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## **Evidence, Benefits and Barriers to Achieving an Integrated Cardioprotective Dietary Pattern**

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**EVIDENCE, BENEFITS AND BARRIERS TO  
ACHIEVING AN INTEGRATED CARDIOPROTECTIVE  
DIETARY PATTERN**

**By Dianne Patricia Reidlinger**

**A thesis submitted to King's College London for  
the degree of Doctor of Philosophy in the Faculty  
of Life Sciences and Medicine**

**Diabetes & Nutritional Sciences Division  
King's College London  
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*In loving memory of Prue.*

## **Publications**

### **Original Research**

Reidlinger, D.P., Darzi, J., Hall, W.L., Seed, P.T., Chowienczyk, P.J. Sanders, T.A.B. (2015) How effective are current dietary guidelines for cardiovascular disease prevention in healthy older men and women? A randomized controlled trial. *Am J Clin Nutr* (epub ahead of print). DOI: 10.3945/ajcn.114.097352

### **Abstracts**

Reidlinger, D.P., Darzi, J., Hall, W.L., Maniou, Z., Govoni, V., Seed, P.T., Chowienczyk, P.J. Sanders, T.A.B. (2013) The effectiveness of an integrated dietary intervention compared with an average UK diet in reducing cardiovascular disease risk factors in older men and women aged 40 to 70 years: the CRESSIDA Study. *Proc Nutr Soc*, 72, OCE4: E249.

Fisk, C.M., Reidlinger, D.P., Sanders, T.A.B. (2013) Advice to consume 1-2 portions of oily fish per week improves vitamin D status. (2013) *Proc Nutr Soc*, 72, OCE4: E188.

Darzi, J., Reidlinger, D.P., Hall, W.L., Maniou, Z., Govoni, V., Taylor, D.R., Seed, P.T., Chowienczyk, P.J. Sanders, T.A.B. (2013) Nutritional biomarkers to assess compliance to dietary advice given in an integrated dietary intervention: results from the CRESSIDA Study. *Proc Nutr Soc*, 72, OCE4: E285.

Reidlinger, D.P., Goff, L., Darzi, J., Govoni, V., Berry, S.E., Hall, W.L., Chowienczyk, P.J. Sanders, T.A.B. (2011) The effect of an integrated dietary intervention (CRESSIDA) on plasma lipids. *Atherosclerosis*, 218, e1.

## Thesis abstract

This thesis investigated the hypothesis that modifying the overall dietary pattern to conform with UK dietary guidelines would lead to significant reductions in cardiovascular risk factors when compared to a conventional UK diet. Two additional studies were undertaken: a qualitative study exploring factors influencing compliance to the dietary intervention and an investigation into whether a cardioprotective dietary pattern is more expensive than a conventional UK dietary pattern.

An integrated dietary intervention consistent with UK dietary guidelines (5 portions of fruit and vegetables per day, increased consumption of whole grain cereals and oily fish; moderate total fat; reduced saturated fat, added sugars and salt intake) was developed. Changes in daytime systolic blood pressure, ratio of total cholesterol to HDL cholesterol, and endothelial function were compared after 12 weeks in healthy adults aged 40 to 70 years following either the cardioprotective diet (n=80) or a representative UK diet (n=82). There was a significant reduction in daytime SBP of 4.2 mmHg and a 4.2% reduction in TC:HDL-C compared to the control diet, however endothelial function did not differ between groups.

Participants randomised to the cardioprotective diet (n=8) were interviewed in a qualitative study. Motivators identified were sociocultural; many specific to the study context. Elements were identified that could be implemented outside of a scientific study environment. Participants adopted a number of strategies in response to social and environmental barriers, some of which would be hard to maintain in the longer term. A retrospective analysis of food records completed by a subset of participants (n=40) found there was no difference in the cost of the two diets at endpoint, nor was there a difference in dietary costs compared to baseline.

The work described suggests that the adoption of a dietary pattern consistent with UK dietary guidelines does improve cardiovascular risk. Cost may not be a barrier to adopting a cardioprotective dietary pattern in individuals who are not specifically of lower socioeconomic status. These findings and factors affecting compliance to the intervention are discussed in relation to the translation beyond the trial setting to inform public health initiatives for cardiovascular disease prevention.

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## List of abbreviations

ABP	Ambulatory blood pressure
AI	Augmentation index
ANCOVA	Analysis of covariance
Apo A1	Apolipoprotein A-1
Apo B	Apolipoprotein B-100
BHS	British Hypertension Association
BMI	Body mass index
BMR	Basal metabolic rate
BP	Blood pressure
CHD	Coronary heart disease
CRP	C-reactive protein
CVD	Cardiovascular disease
DASH	Dietary Approaches to Stop Hypertension
DBP	Diastolic blood pressure
DHA	Docosahexaenoic acid (22:6n-3)
DVP <sub>RI</sub>	Digital volume pulse reflection index
DVP <sub>SI</sub>	Digital volume pulse stiffness index
EPA	Eicosapentaenoic acid (20:5n-3)
FMD	Flow-mediated dilation
GTN	Glycerol trinitrate
HDL	High density lipoprotein
LDL	Low density lipoprotein
MAP	Mean arterial pressure
MUFA	<i>Cis</i> monounsaturated fatty acids
<i>n</i> -3 LCP	<i>n</i> -3 long chain polyunsaturated fatty acids
NDNS	National Diet and Nutrition Survey
NMES	Non-milk extrinsic sugars
PUFA	Polyunsaturated fatty acids

PWV <sub>c-f</sub>	Carotid-femoral pulse wave velocity
RCT	Randomised controlled trial
SBP	Systolic blood pressure
SFA	Saturated fatty acids
TC:HDL-C	Ratio of total cholesterol to HDL cholesterol
TG	Triglyceride
UK	United Kingdom



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## **Statement of contribution**

### **Cardioprotective dietary intervention (Chapter 3):**

The author contributed to the ethics application process and was responsible for the development and delivery of the dietary intervention, including all dietary visits throughout the study, collection and analysis of dietary data, and all tasks related to the provision of food items to participants. In addition, she undertook study team tasks for the day to day running of the study including study recruitment, screening, pre-baseline and baseline data collection, and assisted with other data collection and participant management tasks daily.

Other members of the study team were responsible for: designing and obtaining funding for the study (principal and co-investigators: Professor Tom Sanders, Dr Wendy Hall, Dr Sarah Berry, Dr Phil Chowienczyk) coordinating the study (Dr Wendy Hall), developing the data collection forms and study manual, coordinating recruitment and visit processes (Dr Julia Darzi), vascular outcome measures, storage and transport of samples to King's College Hospital, processing of urine samples and other technical responsibilities (Ms Virginia Govoni), preparation and processing of samples at King's College London (Mr Robert Gray), quality control of vascular measures (Ms Karen McNeill), downloading of blood pressure monitor data (Ms Virginia Govoni, Dr Julia Darzi, Dr Zoe Maniou), endothelial function outcome measures (Dr Benyu Jiang, Ms Louise Watt), data analysis plan and statistics (Mr Paul Seed), clinical biochemistry analysis of samples (Ms Tracy Dew), day to day study administration (Ms Laura O'Sullivan), nursing and management staff at the Clinical Research Facility, St Thomas' Hospital (phlebotomy, governance and use of facilities)..

### **Qualitative investigation (Chapter 4):**

The author was responsible for the design of the study, application to ethics, performed the interviews, checking the transcripts of interviews, and leading the process of data analysis including the development of the themes and their relationships in conjunction with another researcher.

Other people who contributed to this study included Ms Katie Townsend and Dr Louise Goff. Katie Townsend was an undergraduate dietetic student researcher completing her BSc research project. She recruited participants, undertook transcription of the interviews and assisted in the data analysis including the development of the themes. Dr Louise Goff assisted in the design of the study and developing the application to ethics, data analysis including checking the developed themes and interrelationships, and co-supervision of the dietetic student researcher BSc project.

### **Dietary Costing Study (Chapter 5):**

The author contributed to the design of the study in conjunction with a co-researcher and undertook all data collection and data analysis for the study. Dr Louise Goff contributed to the design of the study and approaches to data collection and data analysis as co-researcher.

# Chapter 1 Introduction

Government endorsed food and nutrition recommendations that are mostly focused on chronic disease prevention, known as dietary guidelines, are broadly similar in the economically developed world despite recent debate about what constitutes a healthy diet (Reynolds et al., 2014). The guidance has evolved and increasingly been informed by evidence, predominantly based on epidemiological associations between dietary intakes and clinical endpoints; however there is a growing body of intervention studies. These are usually focused on the manipulation of one or two nutrients only and their effect on risk factors, often in people with established disease. Expert opinion has been crucial to interpret the vast array of evidence, and cultural, social, economic and historical factors have also been influential (Schneeman, 2003). Most recently, there has been a move to food-based dietary guidelines (as opposed to nutrient-based recommendations) reflecting an acknowledgement that consumers are concerned with foods, rather than nutrients (World Health Organization, 1998).

This chapter will explore the relevant literature relating to dietary influences on cardiovascular disease (CVD) prevention, with a focus on the literature supporting the food and nutrient recommendations from the United Kingdom (UK) dietary guidelines. Evidence for interventions to support dietary change will also be introduced.

## 1.1 Cardiovascular disease

Cardiovascular disease is the leading cause of death worldwide (Strong et al., 2005). Cardiovascular disease is a term for what is in fact a continuum of disease, encompassing coronary artery disease (leading to coronary heart disease; [CHD]), cerebrovascular disease (stroke) and peripheral vascular disease (Townsend et al., 2012). Most CVD is a consequence of atherosclerosis affecting large and medium arteries, where clinical events occur as a result of the rupture of an atherosclerotic plaque leading to thrombosis and vessel occlusion or the rupture of a vessel (aneurism) causing haemorrhage. Atherosclerosis is a degenerative inflammatory disease characterised by lipid accumulation in the artery wall (Zhang et al, 2014). It is a chronic condition that develops over a lifetime with the clinical horizon occurring in men after the age of 45 years and ten years later in women (Deanfield et al., 2007).

## 1.2 Atherosclerosis

Atherosclerosis is an inflammatory disease characterised by the accumulation of lipids in the artery wall (Ross, 1999). Although an area of extensive research, the 'response-to-injury' hypothesis, proposed by Ross and Glomset, is widely accepted in the aetiology of atherosclerosis (Ross and Glomset, 1973). High levels of blood cholesterol, in particular LDL cholesterol, are principal risk factors for atherosclerosis. However, atherosclerotic lesions are

thought to be a product of much more than just hypercholesterolaemia, with a series of highly specific processes leading up to the disease (Ross, 1999, Deanfield et al., 2007).

The vascular endothelium is a monolayer of cells lining the blood vessels and is responsible for the homeostatic regulation of the vessel wall and lumen, maintaining vascular tone, blood fluidity and limiting inflammation and smooth muscle cell proliferation (Vita and Keaney, 2002). Various stages in the pathophysiology of atherosclerosis have been identified (Figure 1.1) and the Ross and Glomset hypothesis suggests that endothelial dysfunction (the impairment of endothelial function) heralds the earliest stages in the process of atherosclerosis (Ross, 1999) and is also involved in later stages when clinical symptoms are present (Vita and Keaney, 2002). Intervention studies have demonstrated that endothelial function can be improved through many diverse treatments including lipid lowering therapy, smoking cessation and exercise (Ashor et al., 2015, Reriani et al., 2011, Vita and Keaney, 2002). However, the direct effect of diet on endothelial function remains uncertain (Landberg et al., 2012).

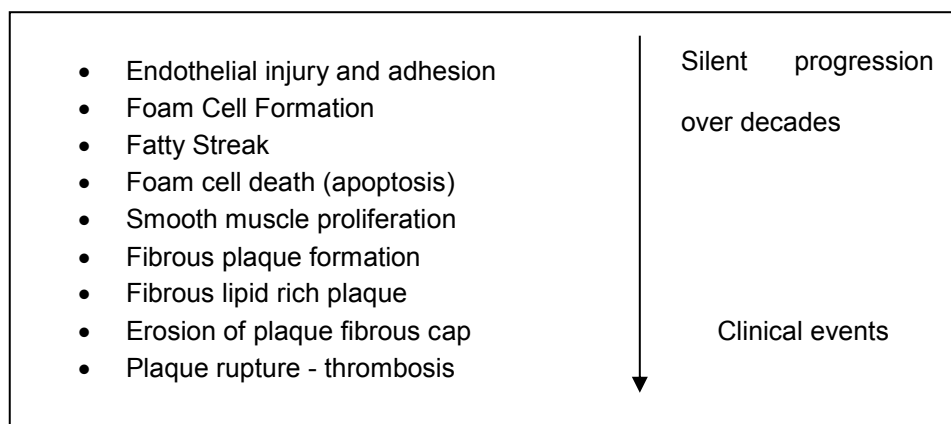


Figure 1.1 Stages of atherosclerosis (Bentzon et al., 2014)

It has been proposed that inflammation is involved in the development of atherosclerosis at every stage – initiation, progression and complications (Pearson, 2003). The endothelial dysfunction that results from the initiating injury leads to compensatory biological responses mediated by monocyte derived macrophages and other immune cells, altering the homeostatic properties of the endothelium including increased adhesiveness and permeability to leukocytes or platelets, promotion of pro-coagulant processes (replacing the anticoagulant properties present in normal endothelium), and the formation of vasoactive molecules, cytokines and growth factors (Ross, 1999). Cholesterol particles become trapped and undergo progressive oxidation, which are then scavenged by macrophages leading to the accumulation of cholesterol esters, resulting in foam cells. Arterial fatty streaks are a result of the accumulation of macrophages engorged with proteins rich in apolipoprotein B100 (apo-B), especially LDL and chylomicron remnants, which then progress to form fibrous plaques. These plaques reduce the arterial lumen, decreasing the capacity to provide oxygenated blood to tissues (Badmny et al., 2014).

## 1.3 Cardiovascular disease risk factors

The development of atherosclerosis has been related to several risk factors, many of which have been demonstrated to be modifiable (Table 1.1) (JBS3, 2014). Age, gender, ethnicity, and family history are associated with cardiovascular risk but are largely non-modifiable. With the evidence building for the Barker Hypothesis (Barker, 1995), birth weight has also been proposed as a risk factor that is potentially modifiable, at least for future generations, if maternal interventions can be implemented.

Historically three behaviourally-influenced risk factors were considered the strongest predictors of CVD risk: cigarette smoking, blood pressure (BP) and total blood cholesterol levels (Kannel et al., 1986). These principal risk factors emerged from early population-based studies, however subsequent cross-sectional studies have been less consistent in explaining the diversity in whole-of-population differences in risk and have highlighted the complexity and inter-related nature of CVD risk factors. The range of accepted risk factors is now broader, spanning biological (including serum cholesterol levels and BP), genetic (including gender, ethnicity and family history), psychosocial (including emotional turmoil and its effect on health-related behaviours, cultural preferences and experiences of chronic stress) (Rozanski et al., 1999, Rozanski et al., 2005) and environmental markers (including differences in socioeconomic status, housing conditions, transport, social organisation, access to health care, and environmental pollutants etc) (Davey Smith et al., 1998). Related behaviours such as smoking, alcohol intake, physical activity (Lahti-Koski et al., 2002, Shaper et al., 1981), and meal pattern habits (Smith et al., 2010, McNaughton et al., 2009) may influence dietary choices through a complex interplay of behavioural factors and preferences which in turn have an impact on risk factors.

Table 1.1 Risk factors for cardiovascular disease

<b>Modifiable risk factors</b>	<b>Non-modifiable risk factors</b>
Blood pressure	Age
Diabetes	Gender
Smoking	Ethnicity
Obesity	Family History
Physical Inactivity	Birth weight
Dyslipidaemia <i>Low HDL cholesterol, high/small dense LDL cholesterol, high triglycerides</i>	

### 1.3.1 Blood lipids and risk

Serum total cholesterol shows a continuous association with CVD risk without threshold (Lewington et al., 2007). Following on from large epidemiological studies such as the Seven Countries study (Keys et al., 1986) that established total cholesterol as a marker of CVD risk,

a more complex picture has emerged whereby specific lipoproteins (in particular high density lipoprotein, HDL; and low density lipoprotein, LDL) and the ratio of total cholesterol to HDL cholesterol (TC:HDL) are now considered a more important predictor of overall CVD risk than total cholesterol alone (Riediger et al., 2010).

LDL cholesterol has an established role in the process of atherogenesis, with universal agreement that lowering LDL cholesterol reduces cardiovascular risk (Di Angelantonio et al., 2009) and is therefore the primary focus for intervention in clinical practice (National Cholesterol Education Program Expert Panel on Detection, 2001). There is good evidence that lowering LDL cholesterol leads to regression of atheroma in randomised controlled trials of statin therapy (Lee et al., 2008, Taylor et al., 2002, Smilde et al., 2001) and in a number of small, intensive dietary intervention trials (Watts et al., 1992, Arntzenius et al., 1985, Ornish et al., 1998).

Conversely, HDL cholesterol is inversely associated with cardiovascular risk in prospective cohort studies (Gordon et al., 1989). Women have higher HDL levels compared to men and are at lower risk of CVD until after menopause when both HDL and the risk advantage declines suggesting higher HDL is protective. The value of interventions with the aim of increasing HDL cholesterol levels is less certain (Di Angelantonio et al., 2009); recent drug intervention trials have cast doubt on the benefits of increasing HDL levels where clinical outcomes are the endpoints (Barter et al., 2007).

Other factors of importance to risk include the size of lipoproteins, in particular elevated small dense LDL particles which are known to be associated with increased risk; and triglyceride (TG) rich lipoproteins (chylomicron and very low density lipoproteins [VLDL]) which are reflected in plasma concentrations of non-HDL cholesterol and apolipoprotein B-100 (apoB) (Watts and Karpe, 2011). The inverse correlation of HDL cholesterol with risk may therefore be more a reflection of the relative presence of other cholesterol remnants, rather than a primary protective effect of HDL.

Elevated TGs are also associated with CVD risk but their role in disease development has been less clear, with questions as to whether raised TGs have an independent effect or whether their risk is modulated by HDL- and LDL-cholesterol levels (Di Angelantonio et al., 2009). As a consequence, TGs have sometimes been considered more a marker of risk than a true risk factor (Miller et al., 2011). Other research suggests that genetic causes of raised TG may be associated with an increased risk of CVD (Triglyceride Coronary Disease Genetics Consortium and Emerging Risk Factors Collaboration, 2010). The combined effect of high TGs, high LDL and low HDL cholesterol, along with increased waist circumference, elevated fasting glucose, and elevated BP are factors contributing to a syndrome of metabolic abnormalities known to be associated with increased CVD risk.

### **1.3.2 Blood pressure and risk**

Aside from blood lipids, BP is considered a major predictor of CVD risk with the risk stronger for stroke than for CHD. In common with lipids, the relationship between BP and risk is linear (Lewington and Clarke, 2005) and without any evidence of a threshold down to at least 115/75 mmHg (Lewington et al., 2002). Treatment of age-related increases in BP is associated with a reduction in cardiovascular events regardless of initial BP (Law et al., 2009). Measurement of BP is therefore an important tool for assessing cardiovascular risk and monitoring changes in vascular function in the clinical setting. It is a continuous variable subject to short term, daytime, diurnal and seasonal variation causing great intra individual variability, and is best characterised by multiple readings under various conditions (Kaplan et al., 2010). Accurate measurement is therefore best performed by ambulatory BP monitoring over a 24-hour period (Keenan et al., 2009).

Structural changes that occur in the arteries as a result of aging include degeneration of elastin, increased collagen and thickening of the arterial wall, along with progressive dilation of the arteries (Sutton-Tyrrell et al., 2005), all leading to a loss of elasticity or 'arterial stiffness'. Pulse wave velocity (PWV) is a measure of arterial stiffness, and is associated with mortality in clinical populations (Boutouyrie et al., 2002). Arterial stiffness is believed to be responsible for the increase in systolic BP (in the absence of an increase in diastolic) that occurs after the age of 60 years (Adji et al., 2011, Burlingame et al., 2009). Arterial stiffness indices are emerging as novel markers of risk particularly for age-related CVD.

### **1.3.3 Obesity and risk (fat distribution, age/ ethnicity)**

Obesity, frequently defined using a body mass index (BMI) cut off of  $\geq 30 \text{ kg/m}^2$ , is widely recognised to be a key risk factor for CVD (World Health Organization, 2000, Poirier et al., 2006). Although excess body weight negatively impacts on BP, blood lipids, and blood glucose, it is also independently associated with an increased incidence of CHD and stroke (Hubert et al., 1983, Poirier et al., 2006).

In the UK, obesity affects a quarter of adults although prevalence is higher in some population groups (Joint Health Surveys Unit et al., 2012). In particular, social disadvantage is related to increased obesity rates (McLaren, 2007, Cohen et al., 2013, National Institute for Health and Care Excellence, 2014c). Educational attainment and income are inversely related to obesity in the UK and there are also ethnic differences in prevalence (El-Sayed et al., 2012, The NHS Information Centre, 2011).

Research into the health consequences of obesity has revealed it to be a heterogeneous condition, with the distribution of excess body fat being an important determinant of overall health risk. Individuals with a high proportion of abdominal fat experience greater incidence of CHD, type 2 diabetes and related morbidity (Després et al., 2001, Poirier et al., 2006). Therefore waist circumference cut offs of 88cm for women and 102cm for men have been

proposed as useful clinical indicators of abdominal fatness and hence CVD risk (Cameron et al., 2010, Lean et al., 1995).

## **1.4 Risk calculation algorithms**

Individuals tend to present with clusters of risk factors for CVD, and the presence of more than one risk factor is additive in the effect on overall risk (Jackson et al., 2005) with absolute differences in risk of more than twenty-fold in people with the same BP or cholesterol levels (Neaton et al., 1992). The follow up to the Framingham Heart Study demonstrated that total serum cholesterol is a poor predictor of risk on its own (Anderson et al., 1987) and research has since highlighted the importance of different fractions of blood cholesterol, notably LDL-cholesterol and HDL-cholesterol (Kannel et al., 1979a, Després et al., 2000, Carmena et al., 2004). It is now recognised that combining multiple risk factors improves risk prediction (Castelli, 1996). Other potential markers of risk, including indices of arterial stiffness, endothelial function and chronic inflammation, have been suggested to mediate risk and may explain some of the variation in mortality and morbidity with blood lipids, BP and smoking.

Risk prediction equations attempt to estimate cardiovascular risk by combining multiple risk factors and converting them into a numeric estimate of risk (Hippisley-Cox et al., 2007). A number of risk prediction algorithms have been developed in an effort to focus CVD prevention efforts, predominantly to identify individuals most likely to benefit from targeted drug interventions, including the Framingham risk equations (D'Agostino et al., 2008, Pencina et al., 2009), the UK-specific QRISK score (Hippisley-Cox et al., 2007), and the JBS3 cardiovascular risk assessment equation (JBS3, 2014). Both Framingham and QRISK equations focus on an individual's 10-year risk of CVD, which allows prevention and treatment efforts to be targeted toward those at highest risk. The recent JBS3 calculator provides 10-year risk as well as a longer-term assessment of risk over an individual's lifetime.

The previous application of the Framingham equations to the UK population was limited by the predominantly White American population it was based on. In addition, estimates of risk were derived from data from a time period when CVD incidence was much greater in the USA (Barzi et al., 2007), likely resulting in a likely significant overestimation of risk in European populations (Brindle et al., 2003) and an underestimation in more deprived populations (Brindle et al., 2005, Tunstall-Pedoe and Woodward, 2006). Of note, social deprivation, family history, BMI and current treatment for hypertension is also not included in the Framingham algorithm (Brindle et al., 2006).

The QRISK score is derived from UK population data including family history, age, gender and deprivation and is therefore more discriminating in determining risk (Hippisley-Cox et al., 2007). The addition of ethnicity in the next iteration of the equation (QRISK2) has further increased its utility (Collins and Altman, 2012, Hippisley-Cox et al., 2008). The very recent Joint British Societies' consensus recommendations for the prevention of CVD (JBS3), which calculates risk from the QRISK database, also includes measures of deprivation and ethnicity,



is specific to the UK population. Furthermore, it has the advantage of providing both 10-year risk for targeted prevention and management of CVD in those at immediate high risk, as well as an estimate of lifetime risk. As 10-year risk is overwhelmingly driven by age and gender, both risk factors that cannot be modified, the addition of the lifetime risk assessment enables preventative action to be taken in those that currently don't receive priority efforts but still have considerable room for risk improvement (JBS3, 2014)

## **1.5 Dietary influences on cardiovascular disease risk**

Much of the evidence assessing the impact of diet on CVD risk is based on epidemiological studies, in which the role of specific nutrients or food components have been identified as well as more integrative aspects of dietary patterns. Such studies have a number of limitations, including variable quality of dietary and outcome data, as well as confounding by unmeasured variables such as activity levels, smoking, sociocultural factors and economic influences. Intervention studies, which target foods and behaviours rather than specific nutrients, are more likely to detect an effect from dietary change. For practical reasons, the majority of intervention studies focus on surrogate markers of CVD risk including serum cholesterol and BP.

The recent global burden of disease study, for example identified eight dietary components as leading risk factors for all-cause disease morbidity (Lim et al., 2012), of which CVD is the leading cause in the UK (GBD 2013 Mortality and Causes of Death Collaborators, 2014). The dietary factors identified were a low intake of fruits, nuts and seeds, whole grains, vegetables and seafood omega 3 fatty acids as well as alcohol use and a high sodium diet (Lim et al., 2012). The current evidence for these dietary factors in manipulating the modifiable risk factors for CVD will now be considered.

### **1.5.1 Dietary fat and cardiovascular disease**

A wide body of research has been undertaken to investigate the role of dietary fat in CVD risk. Much of this has centred predominantly on its impact on blood lipids, however the role of dietary fat in the development of obesity and its strong correlation with hypertension have also been explored. The interpretation of this research has recently become a bed of controversy, due in part to the predominance of epidemiological evidence and because the effect on clinical outcomes has not been undertaken in randomised controlled trials. In addition, the analysis of isolated nutrients is likely to be confounded by a lack of consideration of other nutrients and the overall dietary pattern adding to the current uncertainty around dietary fat and cardiovascular risk.

Acknowledging the considerable research that has since been undertaken, epidemiological evidence for the role of dietary fat in mediating cardiovascular risk began with the Seven Countries Study which found a positive correlation initially between total fat and death from CVD (Keys, 1970). Further analysis revealed that intakes of saturated fat, rather than total fat,

were more strongly correlated with CVD mortality and with blood cholesterol levels which emerged as a modifiable CVD risk factor (Keys et al., 1986, Katan et al., 1997). This led to the diet-heart hypothesis proposing that dietary fat, in particular saturated fat, increased cardiovascular risk through its effect on serum cholesterol levels.

The focus away from total fat was further supported by the observation that a number of countries with higher intakes of fat had lower CVD mortality. One such country was Crete with very low CVD mortality but high population fat intakes (40% energy) sourced predominantly from olive oil which is rich in monounsaturated fatty acids (MUFAs) (Keys et al., 1981). Another notable example was Greenland where the Eskimos had low rates of CVD despite a high fat and cholesterol intake, a significant proportion of which was *n*-3 long chain polyunsaturated fatty acids (*n*-3 LCP) from fish and seal (Bang et al., 1971, Katan et al., 1997). Early metabolic feeding studies of cross-over design confirmed that modifying dietary cholesterol, SFAs, MUFAs and polyunsaturated fatty acids (PUFAs) produced predictable responses in serum cholesterol levels and equations were developed (Hegsted et al., 1965, Keys et al., 1957).

The diet-heart hypothesis has recently become the focus of controversy with a number of systematic reviews and meta-analyses of observational studies concluding that saturated fat is not associated with CVD risk (Skeaff and Miller, 2009, Siri-Tarino et al., 2010). These have been criticised for methodological reasons including inaccurate dietary assessment methods, inadequate sample sizes, regression dilution bias (Skeaff and Miller, 2009, Hooper et al., 2012) and - for one of the reviews (Siri-Tarino et al., 2010) - the adjustment for serum cholesterol levels (Papadopoulou and Stanner, 2014).

A recent Cochrane review of intervention studies comparing reduced and modified fat diets on cardiovascular outcomes and risk factors found no clear effect of any dietary fat intervention on mortality, but a reduction in saturated fat intake was associated with reduced cardiovascular events overall (Hooper et al., 2012). The review supported a small effect on weight and BMI, but no other risk factors, with reduced fat diets. Modified fat diets, by contrast, reduced serum total cholesterol and fasting serum TGs, but had no clear effect on LDL-C, HDL-C, weight or BMI (Hooper et al., 2012).

Polyunsaturated fatty acids of relevance to cardiovascular risk include *n*-6 PUFAs (especially linoleic acid) and *n*-3 fatty acids, particularly  $\alpha$ -linolenic acid (ALA) and the *n*-3 fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) predominantly derived from fish oils. Good evidence from prospective cohort studies support a protective effect of regular fish intake on CVD events (Kromhout et al., 1985, Burr et al., 1989) and a recent review of prospective cohort studies found that *n*-3 fatty acids were associated with a reduction in the risk of CHD (Chowdhury et al., 2014).

Results from intervention studies of fish oil supplementation have been variable but have suggested a modest TG lowering effect at doses approaching usual dietary intakes; higher supplementation levels have also been reported to decrease heart rate and (variably)

endothelial function (Mozaffarian and Wu, 2011). However intervention studies have shown no clear effect, and perhaps even the potential for harm over time, of *n*-3 fatty acids (including from supplements as well as from dietary sources) on CVD endpoints. Effects on risk factors were limited to a reduction in serum TGs and an increase in LDL-cholesterol in a systematic review of the evidence (Hooper et al., 2004).

A widely reported systematic review and meta-analysis of randomised controlled trials also concluded that guidelines encouraging reduced saturated fat and increased polyunsaturated fat could not be supported by current evidence (Chowdhury et al., 2014). However, this review was criticised on a number of fundamental aspects including the use of incorrect data and statistical errors (subsequently corrected), omission of several key studies demonstrating the efficacy of substituting SFA with PUFA and MUFA in lowering LDL-cholesterol (Willett et al., 2014, Te Morenga and Mann, 2014), lack of differentiation between animal and plant sources of MUFA (Schwingshackl and Hoffmann, 2014), and the inclusion of the Sydney Diet and Heart Study which used spreads high in *trans*- fatty acids as part of the intervention (Papadopoulou and Stanner, 2014, Te Morenga and Mann, 2014, Liebman et al., 2014). There was also some dismay that the authors had taken such a reductionist approach: ie a narrow, single-nutrient approach and view of CVD risk as a disorder of lipid accumulation rather than evaluating the evidence in the wider context of dietary patterns and indices of risk such as inflammation and oxidative stress (O'Neil and Itsiopoulos, 2014). A more recent review which includes updated data, was more supportive of dietary guidelines recommending the replacement of SFA with PUFA for reducing cardiovascular risk

In summary, despite the controversy it is generally accepted that substituting different fatty acids, including SFA, have varied effects on total, LDL and HDL cholesterol. The reduction of dietary saturated fat may improve overall CVD risk if replaced with *cis*-monounsaturated or polyunsaturated fats (Mozaffarian et al., 2010). *Trans*- fatty acids result in increased LDL cholesterol, in a linear dose-response relationship, when compared to *cis*-monounsaturated and polyunsaturated fats (European Food Safety Authority and Panel on Dietetic Products, 2010). Conversely numerous studies have demonstrated that replacing saturated fat with carbohydrate results in an increase in TGs, reduction in HDL cholesterol, and competing changes in total, LDL and TC:HDL-C (Burlingame et al., 2009). Dietary cholesterol results in a relatively small effect on serum total and LDL cholesterol in most individuals, however there is some evidence of a link between SFA, trans fatty acids and dietary cholesterol (Sanders, 2009). Revised predictive equations from a meta-analysis of 27 feeding trials were developed, which attempted to account for the differing effects of replacement nutrients where SFA are reduced (Mensink and Katan, 1992). Since then, further trials have elucidated the specific effects of different fatty acids and a meta-analysis undertaken by the European Food Standards Agency (EFSA) showed that individual SFA varied in their effect on total, LDL and HDL cholesterol (European Food Safety Authority and Panel on Dietetic Products, 2010) (Table 1.2).

Table 1.2 Summary of predicted change in serum lipids from replacing 1% energy by individual fatty acids for carbohydrate, and from increasing intake of dietary cholesterol by 100 mg

	Total Chol	LDL-Chol	HDL-Chol	TC: HDL-C
<b>Lauric acid (12:0)</b>	+	+	+	-
<b>Myristic acid (14:0)</b>	+	+	+	-
<b>Palmitic acid (16:0)</b>	+	+	+	+
<b>Stearic acid (18:0)</b>	-	-	+	-
<b>Elaidic acid (18:1 <i>trans</i>)</b>	+	+	No effect	+
<b>Oleic acid (18:1 <i>cis</i>)</b>	-	-	+	-
<b>PUFA</b>	-	-	+	-
<b>Dietary cholesterol (+100 mg/day)</b>	+	+	+	+

+ (-) 0.00 to <0.01 mmol/l; + + (- -) 0.01 to <0.03 mmol/l; + + + (- - -) 0.03 to < 0.05 mmol/l; + + + + (- - - -) ≥ 0.05 mmol/l

Total Chol, total cholesterol; LDL-Chol, low density lipoprotein cholesterol; HDL-Chol, high density lipoprotein cholesterol; TC:HDL-C, ratio of total to high density lipoprotein cholesterol.

*Data presented represents mean change from replacing 1% energy by individual fatty acids for carbohydrate based on a meta-analysis [adapted from (European Food Safety Authority (EFSA), 2004)] and changes from increasing intake of dietary cholesterol by 100 mg based on analysis of (Weggemans et al., 2001). Table adapted from (Sanders, 2009).*

There is good evidence that high fat meals postprandially impair endothelial function, although these effects may be ameliorated through dietary protein (Djoussé et al., 1999). Chronic dietary fat consumption is less straight forward. Long chain omega 3 PUFAs (EPA and DHA) may reduce arterial stiffness although studies are conflicting (Hall, 2009). A well conducted double blind randomised trial using fish oil capsules with EPA and DHA doses equivalent to one, two and four portions of oily fish per week found no effect on endothelial function at any dose (Sanders et al., 2011). Another intervention trial comparing diets high in either SFA or MUFA or a high carbohydrate diet found no influence of any of the diets on endothelial function (Sanders et al., 2013). Other evidence from randomised trials suggest that *trans* fatty acids may impair endothelial function although there is insufficient evidence of any other differences with monounsaturated, polyunsaturated or saturated fatty acids (Hall, 2009).

Despite clinical trials demonstrating an impact on serum cholesterol levels with increased intakes of dietary cholesterol (Table 1.2), epidemiological studies do not support a link between dietary cholesterol and clinical endpoints (Dawber et al., 1982, Howell et al., 1997, Hu et al., 1999, McNamara, 1997, Esrey et al., 1996, Krumholz et al., 1994). Dietary cholesterol has been linked to higher BP in ecological studies. For example the Multiple Risk Factor Intervention Trial, a cross sectional study (Stamler et al., 1996), and more recently researchers in another cross sectional study, INTERMAP, found an average increase of

1mmHg in systolic BP for hypertensive individuals with higher dietary cholesterol intakes (Sakurai et al., 2011).

Current UK population recommendations are for total fat intakes to be less than 35% dietary energy (Department of Health, 1994), to reduce intake of saturated fat to less than 10% energy, and replace it with polyunsaturated and monounsaturated fatty acids. By contrast, EFSA recommendations take a somewhat less quantitative approach, instead including more general statements to reduce SFAs to as low as possible, with no recommendation for MUFAs, and advice to include at least 250mg/day of *n*-3 fatty acids for optimal health (European Food Safety Authority and Panel on Dietetic Products, 2010). There is no recommended limit for dietary cholesterol intakes.

### **1.5.2 Dietary fibre, whole grains and cardiovascular risk**

Epidemiological evidence suggests dietary fibre intake is inversely associated with both CHD and stroke, and risk factors for CVD are also less common at the highest intakes (Anderson et al., 2009). In a recent meta-analysis of cohort studies, dietary fibre intake was inversely related to CVD, with each 7g increase in total dietary fibre equating to a risk ratio of 0.91 (Threapleton et al., 2013) supporting an earlier meta-analysis with similar findings (Anderson et al., 2009). Although ecological evidence supports a protective effect of dietary fibre, data from randomised controlled trials, which have been few and relatively short term, are mixed. The results from an early secondary prevention randomised controlled trial failed to find any benefit in increased dietary fibre on clinical outcomes over a two year period (Burr et al., 1989). Short term interventions have failed to find an effect of increased fibre on HDL cholesterol (Yanai et al., 2014), but a small study found increasing dietary fibre improved indices of inflammation (Johansson-Persson et al., 2014).

A whole grain contains the entire edible parts of the grain kernel including the endosperm, germ and bran (Kelly et al., 2009) although a consensus definition of 'whole grain' has yet to be decided. Whole grains contain a number of nutritional and non-nutritional constituents that are likely to be beneficial to human health including dietary fibre, resistant starch, antioxidants, phytoestrogens, vitamins and minerals (Slavin, 2003).

Evidence from prospective cohort studies of whole grains and CVD incidence and risk factors suggests benefits from their intake that are similar to that of fibre, although other micronutrients and non-nutritive effects may confer additional benefits (Anderson, 2004). Higher intakes of whole grains have been associated with reduced CVD mortality and events in several epidemiological studies (Jacobs et al., 1998, Liu et al., 1999, Steffen et al., 2003, Jacobs et al., 1999). Whole grain intakes have also been inversely associated with total cholesterol, LDL cholesterol and body weight (McKeown et al., 2002, Koh-Banerjee et al., 2004, Liu et al., 2003, Bazzano et al., 2005, van de Vijver et al., 2009, Mozaffarian et al., 2011).

Intervention studies on the effects of consuming a diet rich in whole grains are surprisingly limited. A recent meta-analysis of 21 randomised controlled trials concluded that whole grain interventions were effective in reducing fasting glucose, total and LDL-cholesterol (Ye et al., 2012). This review was criticised for pooling studies of interventions with differing whole grains, which introduces considerable heterogeneity into the analysis (Wolever, 2013). An earlier Cochrane review of intervention studies concluded that oatmeal resulted in lower total and LDL cholesterol levels, but there was insufficient evidence for other whole grains and cardiovascular risk factors (Kelly et al., 2009).

Small intervention studies suggest that a diet rich in whole grains may confer benefits in large bowel health including favourable changes to gut microbiota which may have an impact on cardiovascular health (Tuohy et al., 2014), improved insulin sensitivity and postprandial blood glucose response (Jenkins et al., 1988, Liese et al., 2003), and other cardiovascular benefits such as improved blood lipids (Kelly et al., 2009), reduced BP (Tighe et al., 2010, Pins et al., 2002) and the prevention of impaired postprandial vascular reactivity after a high fat meal (Slavin, 2003). The evidence is conflicting, with some trials finding no benefits of whole grain intake on insulin sensitivity, inflammatory markers, BP or body weight (Giacco et al., 2013, Harris and Kris-Etherton, 2010).

In the UK, there is currently no quantitative guidance for whole grain intake. However, the 'Eatwell Plate' recommends that bread, rice, pasta and other starchy foods should comprise around a third of daily food intake and advises that whole grain varieties should be chosen where possible (Public Health England, 2014).

### **1.5.3 Salt and cardiovascular disease**

Observational studies have consistently demonstrated an association between dietary salt (sodium chloride) intake and BP, however the lack of adjustment for confounders such as age, gender, ethnicity, BMI and macronutrient intake in cross sectional and prospective cohort studies limits the strength of the association. A large number of randomised controlled trials have investigated the impact of reduced dietary salt on BP and it is now generally accepted that excessive salt intake has a role in the pathogenesis of elevated BP (Appel et al., 2011). A meta-analysis of such trials demonstrated significant reductions in systolic/diastolic BP of 2.4/1.0 mmHg in normotensive individuals and 5.4/2.8 mmHg in hypertensive individuals was associated with salt restriction (He et al., 2013). Despite many randomised controlled trials demonstrating BP benefits of dietary salt restriction, the optimal recommendation for population salt intakes is still uncertain (Oparril, 2014).

Whilst there is relative consensus on the benefits of reducing dietary salt in terms of BP (for people who do not have heart failure), the reported effects on blood lipids have been inconsistent. A Cochrane systematic review and meta analysis of randomised controlled trials comparing low- versus high-sodium intake concluded that salt reduction had the CVD risk-increasing effect of increasing serum cholesterol and TG concentrations (Graudal et al., 2012).

However another review which assessed the impact of reducing salt intakes in non-acutely ill people, found that there was no adverse effects on blood lipids (Aburto et al., 2013b).

A further area of controversy relates to a Cochrane review investigating the cardiovascular effects of reduced dietary salt intake. Whilst the review concluded that modest BP lowering from salt reduction was observed, statistical significance was not reached in the meta analysis (Taylor et al., 2011). The analysis was criticised for the inclusion of trials of low sodium diets in people with heart failure (Arcand and Newton, 2012) and for failing to pool studies in hypertensive and normotensive populations, thus reducing statistical power (Neal et al., 2013, He and MacGregor, 2011). It, and another review (DiNicolantonio et al., 2013), have since been withdrawn because two of the included heart failure studies had duplicated data (Francis, 2013). Whilst a well conducted long term trial may resolve unequivocally the question of the benefits or otherwise of dietary salt reduction, to power such a trial would require around 28,000 participants randomised to a low or high salt diet for at least five years (He and MacGregor, 2011) and would be logistically, financially and ethically impractical (Appel et al., 2011).

The current UK guidance on salt intake comes from the SACN review on salt and health which recommended reductions in the UK population salt intake to an average of 6g/ day in adults (SACN, 2003). The target of 6g per day has been set with a timeframe of 2015, with further reductions to 3g/ day proposed by 2025 (National Institute for Health and Care Excellence, 2014d).

#### **1.5.4 Added sugars and cardiovascular disease**

Early epidemiological evidence suggested an association between increased intakes of added sugars and CVD (Yudkin, 1964) and more recent evidence from a cross sectional study in the US would appear to corroborate the hypothesis that higher sucrose consumption confers increased risk for CVD mortality (Yang et al., 2014). However a recent systematic review of evidence identified only three recent prospective cohort studies for inclusion (and a further three older studies), and did not find an association between sugars and CVD events in any of the studies (Nutritional Epidemiology Group University of Leeds, 2012). Similarly, the review included a number of randomised controlled trials using surrogate markers of risk as outcomes, and found no effect of sugars intake on blood TGs and total-, LDL-, HDL-cholesterol nor on BP (Nutritional Epidemiology Group University of Leeds, 2012).

Despite the lack of association with total sugars intake, some of the epidemiological evidence suggests a potential link between sugar-sweetened beverage intake and metabolic syndrome (Malik et al., 2010) with another recent meta-analysis finding a strong positive association with type 2 diabetes, although there was high heterogeneity between studies and the association was reduced after adjustment for BMI (Greenwood et al., 2014). However, the ecological evidence for a relationship with BMI or body fatness is conflicting, and overall there was no association found from cohort studies but randomised controlled trials did suggest a

detrimental link with BMI in a recent systematic review (Nutritional Epidemiology Group University of Leeds, 2012).

The growing interest in the possible negative health effects of added sugars has coincided with reviews of public health guidance recommending that the proportion of energy derived from added sugars in healthy diets should be reduced. The World Health Organisation has proposed that free sugars should provide no more than 5% of total energy intake, a reduction of 5% from previous guidance (World Health Organisation, 2014); however the UK recommendation has remained relatively similar, restricting free sugars to no more than 10% of total energy intake following a review by the Science Advisory Committee of Nutrition (SACN) (Scientific Advisory Committee on Nutrition, 2011) (Scientific Advisory Committee on Nutrition, 2014).

### **1.5.5 Fruit and vegetables and cardiovascular disease**

Several prospective cohort studies have suggested a protective effect of fruit and vegetable intake on stroke and CHD (Bazzano et al., 2002, Joshipura et al., 1999, Hirvonen et al., 2000, Johnsen et al., 2003, Sauvaget et al., 2003, Steffen et al., 2003, Keli et al., 1996). A meta-analysis of these studies concluded that consuming three to five serves of fruit and vegetables was associated with a reduced risk of stroke (relative risk of 0.89) and greater protection (relative risk of 0.74) was noted at intakes of more than five servings, when compared with individuals who consumed less than three servings per day (He et al., 2006). A similar meta-analysis with CHD endpoints found a 17% reduction in risk when comparing intakes of less than three servings of fruit and vegetables per day with intakes of greater than five serves (He et al., 2007). An analysis of fruit and vegetable intakes and deaths from ischaemic heart disease in the EPIC-Heart study, a large observational study across eight European countries, estimated that every 80g portion of fruit and vegetables was associated with a 4% reduction in risk (Crowe et al., 2011).

Epidemiological studies do not offer causal explanations, and it has been postulated that high intakes of fruit and vegetables are a marker of other lifestyle factors rather than conferring a reduced risk directly. The biological mechanisms for the effect of fruit and vegetable consumption in reducing CVD risk is still not known, and good quality evidence is lacking. A recent systematic review and meta-analysis of intervention studies reported on 11 included randomised controlled trials on the effect of increasing fruit and vegetable intake on nutrient outcomes (but not surrogate or clinical outcomes) (Fulton et al., 2014). It concluded that increased fruit and vegetable consumption resulted in greater micronutrient, carbohydrate and fibre intakes, and possibly reduced fat intake, with no overall effect on energy intake. The authors proposed that the health benefits associated with fruit and vegetable consumption could be mediated through an improvement in overall dietary quality in combination with improved micronutrient intakes (Fulton et al., 2014).



Dietary potassium, predominantly found in fruit and vegetables, has been inversely associated with BP in several observational studies and has been proposed as one of the factors that may mediate cardiovascular risk. Other factors being investigated include dietary nitrates; and the large number of bioactive compounds found in plant based foods, including flavonoids.

Prospective cohort studies support an inverse association between potassium intakes and rates of stroke, but the association with CHD and all CVD is less certain (D'Elia et al., 2011). Small but clinically significant inverse correlations between potassium and BP have been supported (Khaw and Barrett-Connon, 1988, Kieneker et al., 2014). However, randomised controlled trial evidence for the protective effect of potassium supplementation and/or fruit and vegetables has yielded conflicting results (Berry et al., 2010, Dickinson et al., 2006). A randomised controlled trial comparing 20 and 40 mmol potassium supplementation with equivalent intake from fruits and vegetables in people with early hypertension did not find a BP lowering effect (Berry et al., 2010) suggesting potassium in amounts similar to five portions of fruit and vegetables per day is insufficient to produce BP lowering effects. Meta-analyses of such trials have been problematic, possibly because of the heterogeneity of included studies particularly in the amount of potassium used for intervention and control groups across different studies (Bates, 2012). However three such meta-analyses found an inverse relationship between potassium intake and BP in non-hypertensive and hypertensive people (Cappuccio and MacGregor, 1991, Whelton et al., 1997, Geleijnse et al., 2003). A more recent meta-analysis reported similar findings for people with hypertension, but found no effect in non-hypertensives (Aburto et al., 2013a).

Dietary nitrates have recently been proposed as a potential mechanism, through a BP lowering effect possibly mediated by the effects of nitric oxide on the vascular endothelium. The intake of nitrate rich foods results in the bioconversion of nitrates to nitrite by oral bacteria; the saliva then carries the nitrite to the acidic environment of the stomach where it is reduced to nitrous acid and subsequently decomposes into nitric oxide and other bioactive nitrogen oxides (Lundberg et al., 2004). The predominant source of dietary nitrates in the UK is vegetables, which range in nitrate content according to the plant family they belong to as well as environmental and agricultural factors (Hobbs et al., 2013, Lundberg et al., 2004). Intervention trials have predominantly demonstrated acute effects on blood pressure and, although promising, the human research to date is still inconclusive (Hobbs et al., 2013).

Flavonoids, and similar biological compounds, have also been proposed as potential mechanisms for the cardiovascular benefits of fruit and vegetable consumption. They are biologically diverse and abundant dietary compounds found in fruit and vegetables, as well as other plant based foods including tea, coffee, red wine and cocoa. Prospective cohort studies suggest an inverse association of flavonoids intake with cardiovascular disease mortality, although the considerable heterogeneity in flavonoid classes investigated, as well as the populations, outcomes and length of follow up hinder attempts at meaningful synthesis of the evidence (Peterson et al., 2012). Similar issues in synthesising randomised controlled trial

evidence has also been reported (Kay et al., 2012) along with the overwhelming complexity of flavonoid classes and their coexistence within individual foods (Hollman, 2014). A recently published rigorous randomised controlled trial comparing a high flavonoid fruit and vegetable dietary intervention with a low flavonoid fruit and vegetable group and a control group which maintained habitual dietary intake suggested modest improvements in CVD risk markers with benefits at around 7 portions of fruit and vegetables per day (Macready et al., 2014). The displacement of other, less health promoting, foods has also been proposed as a potential mechanism for the cardiovascular benefits of fruit and vegetable consumption (Murphy, 2014).

The dietary guidance for the UK population is to consume at least five portions (400g) of fruit and vegetables each day, which excludes potatoes and restricts beans and pulses to a maximum of one portion per day. In addition, 150ml or more of fruit and vegetable juices are included as a maximum of one portion of fruit and vegetables per day, regardless of the amount consumed (Public Health England, 2014).

### **1.5.6 Obesity and cardiovascular disease**

Obesity, particularly central obesity, is a defining feature of the metabolic syndrome and is linked to dyslipidaemia, BP, insulin resistance, and a pro-inflammatory state which are all modifiable risk factors for CVD (Aucott et al., 2011, Barrett and Watts, 2003). It is also an independent risk factor in its own right, and has detrimental effects on the physiological structure and function of the heart (Poirier et al., 2006). Hyperlipidaemia and hypertension increase with progressively increasing BMI, and the two risk factors often appear together thus multiplying the impact of obesity on cardiovascular risk (Brown et al., 2000).

High blood cholesterol and elevated TGs have been associated with obesity in prospective cohort studies (Kannel et al., 1979b), and weight loss in people who are overweight has been shown to improve these risk factors (Dattilo and Kris-Etherton, 1992). Obesity is also linked to lower HDL cholesterol (Brown et al., 2000, Kannel et al., 1979b), although the effect of weight loss on this protective factor is less certain and may be negative (Kelley et al., 2012). There is good evidence from randomised controlled trials that weight loss results in a decrease in serum total cholesterol, LDL cholesterol and TGs, and smaller reductions in HDL cholesterol in the obese population (Poobalan et al., 2004). Trials in non-obese people show more modest effects, however these effects are not maintained in longer term follow up (Aucott et al., 2011).

There is also consistent evidence from observational studies that obesity is associated with altered arterial homeostasis and endothelial dysfunction (Poirier et al., 2006), however the results of intervention studies do not consistently support a role for weight loss in improving endothelial function (Kerr et al., 2011). There is however good evidence from both observational and clinical trials that weight is associated with BP (Appel et al., 2006), and systolic and diastolic BP are strongly correlated with BMI (Savica et al., 2010). Intervention studies have also demonstrated a reduction in BP with weight loss, irrespective of whether a BMI in the 'healthy range' ( $18.5 - 25 \text{ kg/m}^2$ ) is achieved. Based on a meta-analysis of 17 trials,

it has been estimated that a weight loss of 5.1 kg can reduce systolic and diastolic BP by 4.4 and 3.6 mmHg, respectively (Neter et al., 2003) and further benefits are experienced with greater weight loss (Appel et al., 2006).

The evidence to date for the benefits of weight loss has focussed predominantly on improving *risk factors* as opposed to incident cases and mortality rates; further research is needed to determine the benefits of weight reduction on clinical outcomes (Harrington et al., 2009). It is very likely that dietary modification and physical activity exert independent reductions on blood lipids and pressure conferring additional benefits to individuals using these strategies for weight loss.

### **1.5.7 Integrated dietary approaches, dietary patterns and cardiovascular disease**

Epidemiological and intervention studies support the association between dietary patterns and better cardiovascular health, and there has been increasing recognition of the value of looking at whole dietary patterns, rather than individual dietary factors in isolation. Such an approach is more transferable to clinical and public health practice, and allows the interaction, potentially cumulative effect and confounding between different combinations of foods and nutrients to be evaluated (United States Department of Agriculture, 2014). Whilst evidence on individual factors is still useful in understanding their effects on health, dietary pattern research is important to understand how the different combinations and interactions between these factors can impact on CVD risk. A useful definition of 'dietary pattern' has recently been proposed as "the quantities, proportions, variety, or combination of different foods, drinks, and nutrients (when available) in diets, and the frequency with which they are habitually consumed" (United States Department of Agriculture, 2014).

Early observational studies identified a plant based diet as being protective of a number of CVD risk factors suggesting that vegetarian and vegan populations were characterised by lower blood total-, LDL- and VLDL-cholesterol (Burslem et al., 1978, Thorogood et al., 1987), blood TGs and BP (Melby et al., 1994, Appel et al., 2006). The Seven Countries Study noted marked differences in CVD rates across countries, with the lowest prevalence on the island of Crete where it was noted that olive oil and a diet rich in plant based foods predominated (Keys et al., 1981).

Although the majority of evidence for dietary patterns comes from prospective cohort studies, a number of well conducted randomised controlled intervention studies have been undertaken. One of the first and most notable of these studies was the Lyon Diet Heart Study which drew on the findings of Keys et al and tested the efficacy of a Mediterranean diet in people with a history of myocardial infarction, and found dramatic and significant reductions in fatal and non fatal myocardial infarction as well as a reduction in angina, stroke and hospital admissions (De Lorgeril et al., 1994, Renaud et al., 1995). The 'Dietary Approaches to Stop Hypertension' (DASH) study demonstrated the efficacy of an adapted version of the Mediterranean diet in a

controlled feeding study with healthy pre-hypertensive people (Appel et al., 1997) suggesting the approach might be as useful in primary as well as secondary prevention. In a follow up to the DASH randomised controlled trial, the DASH-Sodium trial compared the DASH diet to a typical American diet at three levels of sodium intake (high, intermediate and low), and found additional BP reduction with lower sodium intakes (Sacks et al., 2001) with no adverse effects on blood lipids (Harsha et al., 2004). Although universally accepted as an optimal dietary pattern for cardioprotection, the DASH diet has been assessed against surrogate markers of risk, and has not been rigorously tested with clinical endpoints.

The 'DASH diet' dietary pattern (Table 1.3) has been evaluated in different settings, including a community based setting which did not use the controlled feeding methods of the preceding studies (Appel et al., 2003, Blumenthal et al., 2010), as well as different population groups (Michalsen et al., 2006, Nowson et al., 2009). The DASH diet has similarities to the Mediterranean diet, and emphasises a pattern of high intakes of fruit, vegetables and low fat dairy products. It advocates whole grains, poultry, fish and nuts with less red meat, sweets and sugar sweetened beverages (Appel et al., 1997). The pattern translates into increased fibre, essential fatty acids, antioxidants, lower glycaemic index carbohydrates, and potassium; concurrent with a reduction in saturated fat, cholesterol, sodium and higher glycaemic index carbohydrates. It has been proposed that the diet also results in increased intakes of inorganic nitrate, which may make a contribution to the benefits seen with the intervention (Hord et al., 2009). Overall the DASH diet has been shown to lower BP and improves blood lipid profiles, and is most effective when combined with a reduced sodium intake (Miller et al., 2006). Multiple observational studies have demonstrated the DASH dietary pattern, where compliance is good, to be associated with lower cardiovascular risk (Dietary Guidelines Advisory Committee, 2010).

Table 1.3 Summary of intervention and control diets: DASH dietary studies\*

<b>Dietary component</b>	<b>DASH diet (portions/day)</b>	<b>Fruit and vegetables control diet (portions/day)</b>	<b>Typical American control diet (portions/day)</b>
Fruits including juice	5.2	5.2	1.6
Vegetables	4.4	3.3	2.0
Grains	7.5	6.9	8.2
Low fat dairy	2.0	0.0	0.1
Regular dairy	0.7	0.3	0.4
Nuts, seeds & legumes	0.7	0.6	0.0
Meat	0.5	1.8	1.5
Poultry	0.6	0.4	0.8
Fish	0.5	0.3	0.2
Snacks/ sweets	0.7	1.4	4.1
Fats, oils, salad dressings	2.5	5.3	5.8

\*DASH (Dietary Approaches to Stop Hypertension) dietary studies: (Appel et al., 1997, Sacks et al., 2001, Appel et al., 2003)

Although the Mediterranean diet is less defined, it originates from Southern Mediterranean areas such as Sicily and Greece and is commonly characterised by vegetables, fruit, wheat-based bread and cereal foods, nuts and olive oil, and fish. Several randomised controlled trials have demonstrated improved cardiovascular risk with a Mediterranean dietary intervention (Esposito et al., 2004, Kris-Etherton et al., 2001, Athyros et al., 2011, Wardle et al., 2000, Konstantinidou et al., 2010). The results of a large randomised controlled trial with clinical end points were recently published, which supports the efficacy of the Mediterranean diet in reducing CVD events including deaths (Estruch et al., 2013).

A further leading dietary pattern, known as the 'dietary guidelines' pattern (United States Department of Agriculture, 2014), has recently emerged in the literature as a result of healthy eating scores assessing adherence to population dietary recommendations (Akbaraly et al., 2011, Guenther et al., 2013, McNaughton et al., 2008). Diets scoring highly on these indices are more consistent with government recommendations, and have been related to lower CVD mortality and morbidity (United States Department of Agriculture, 2014, Akbaraly et al., 2011) and inversely related to cardiometabolic risk factors (McNaughton et al., 2009). Other dietary patterns have been studied, for example low fat diets, but with conflicting results (Ornish et al., 1998) (Howard et al., 2006). A summary of robust dietary pattern intervention trials is presented in Table 1.4.

Table 1.4 Summary of randomised controlled trial assessing multiple nutrient target dietary interventions (dietary patterns)

Reference	Population details		Study details						
	Country	Target Group	Design	Dietary intervention	Intervention delivery components	Control/ comparators	Intervention Length	Dietary assessment	Outcomes
<b>Low Fat Dietary Pattern Trials</b>									
<b>Hutchison et al 1983</b>	USA	Male and female adults between 45 and 73 years and diagnosed with peripheral vascular disease (PVD)	RCT	<b>Low fat, high fibre, complex carbohydrate diet (Pritikin Maintenance Diet) group</b> (n=25): Target nutrient intakes: 70-75% calories from carbohydrate, 15-20% calories from protein, 5-10% calories from fat, 40-45g fibre/1000kcal.	Both groups given extensive, personalised small-group dietary instruction and advice to increase exercise and reduce smoking.	<b>AHA Hyperlipidaemia Diet C (control) group</b> (n=20): Target nutrient intakes were 50-55% calories from carbohydrate, 15-20% calories from protein, 25-30% calories from fat (PUFA to SFA ratio of 1.7) and 25-30g fibre/1000kcal.	12 months	48 hour dietary recalls monthly for first 8 months and then at month 10 and 12.	Blood lipids (total, HDL, LDL cholesterol and TGs); ankle-brachial systolic BP ratio, pulsatility index, transit time, treadmill walking distance, % ankle systolic BP drop.
<b>Ornish et al 1990</b>	USA	Males and females aged 35-75 years with coronary artery disease	RCT	<b>Low fat vegetarian diet group</b> (n=22): unrestricted fruit, vegetables, legumes, soybean products, avoidance of all animal products except egg whites and one cup/d non fat milk or yoghurt. Nutrient targets: 10% calories from fat, 15-20% calories from protein, 70-75% calories from complex carbohydrates. Eliminate caffeine and limit alcohol to $\leq 2$ units/day. Restrict salt for hypertensive participants only. Participants supplemented with Vitamin B12. Daily stress management and individualised exercise were prescribed.	<u>Low fat vegetarian diet group</u> : Week long residential education intervention after randomisation, followed by twice weekly 4h-long group sessions facilitated by clinical psychologist.	<b>Control group</b> (n=19): Not asked to make lifestyle changes, but were free to do so.	1 year  <i>Similar outcomes also reported in a separate manuscript after 5 years, with n=20 in the low fat veg group and n= 15 in the control group.</i>	3 day diet diary at baseline and after 1 year. A diary to record exercise and stress management technique compliance was also kept.	Coronary artery lesions analysed by quantitative coronary angiography, HDL-cholesterol, apo A, TC:HDL

Reference	Population details		Study details						
	Country	Target Group	Design	Dietary intervention	Intervention delivery components	Control/ comparators	Intervention Length	Dietary assessment	Outcomes
Howard et al 2006  Women's Health Initiative RCT	USA (40 centres)	Postmenopausal women aged 50 – 79 years, with a baseline diet containing total fat at ≤ 32% of energy . Excluded people who frequently consumed food away from the home.	RCT	<b>Low Fat Diet Group</b> (n=19541): Dietary change with goal of total fat at 20% of energy (presumption that this would reduce SFA to 7% energy); fruit and vegetables at least 5 serves/day; grains at least 6 serves/day.  Participants could participate concurrently in the hormone therapy trial of the WHI, and after 12 months were invited to participate in a trial of calcium and Vit D supplementation.	<u>Low fat diet group</u> : 18 group sessions with nutritionist in first year, then maintenance sessions every 3 months; individual session 12-16 weeks following randomisation. Optional peer-led monthly meetings also offered. <u>Control group</u> : Received a copy of the Dietary Guidelines for Americans and other health related material, but no contact with nutritionists.	<b>Control Group</b> (n=29294): Usual diet.  Participants could participate concurrently in the hormone therapy trial of the WHI, and after 12 months were invited to participate in a trial of calcium and Vit D supplementation.	Follow up at years 3, 6 and 9.	Both groups: FFQ at baseline and after 1 year; 1/3 also completed an FFQ each year in a rotating sample. 4 day food diaries were completed prior to randomisation. Plasma total carotenoids on 6% subsample at year 3. Serum total cholesterol also used as proxy markers fat intake.	1: Breast cancer, colorectal cancer  2: Fatal and non fatal CHD, fatal and non fatal stroke, CVD (composite of CHD and stroke).
<b>Mediterranean Dietary Pattern Trials</b>									
de Lorgeril et al 1994  Renaud et al 1995  Lyon Diet Heart Study	France	Male and female adults aged less than 70 years who had suffered a myocardial infarction in the previous 6 months.	RCT	<b>Mediterranean, α-linolenic acid rich diet group</b> (n=302): more bread, more root and green vegetables, more fish, less meat (beef, lamb, pork replaced by poultry), no day without fruit, replace butter and cream with study margarine (similar fatty acid profile to olive oil but with higher linoleic and α-linolenic acid content). Recommended oils were rape seed oil and olive oil exclusively. Moderate alcohol consumption with meals was allowed.	<u>Mediterranean group</u> : one hour individual session by research cardiologist and dietitian; provided with margarine.  <u>Control group</u> : No dietary advice apart from what would already be provided by hospital dietitian and attending physician.	<b>Prudent diet (control)</b> (n=303): 'Usual diet' post MI	Mean of 27mths (trial stopped early)	24 hour recall and food frequency questionnaire at baseline and at each follow up for Mediterranean diet group only.  Control group: dietary assessment not taken at baseline and occurred once only, four years after commencement.	1: Death from CVD and non fatal acute myocardial infarction 2: Coronary bypass surgery, angioplasty and complications from these

Reference	Population details		Study details						
	Country	Target Group	Design	Dietary intervention	Intervention delivery components	Control/ comparators	Intervention Length	Dietary assessment	Outcomes
<b>Wardle et al 2000</b>	UK		RCT	<p>1. <b>Mediterranean diet</b> (n=61): increase intake of fruit and vegetables, and oily fish and to reduce fat to 30% of energy with substitution of predominantly monosaturated fat for saturated fat.</p> <p>2. <b>Low fat diet</b> (n=59): &lt;20% calories from fat, reduce SFA sources and replace with PUFA sources</p>	<p><u>Mediterranean and low-fat diet groups</u>: 8 education sessions (individual and group) delivered by a dietitian and psychologist on dietary changes required and including a cognitive behavioural component.</p> <p>Provided with spreads and oils high in MUFA (Mediterranean diet group) or PUFA (low fat diet group).</p>	<b>Waiting list (control) diet</b> (n=56):	12 weeks	7 day diet diary at baseline and endpoint. A number of psychological tests were completed at the same timepoints.	Psychological factors; and blood lipids (total, LDL and HDL cholesterol, and TGs)
<b>Singh et al 2002</b>	India	Males and females aged over 25 years with at least one: hypercholesterolaemia, hypertension, diabetes, angina or past myocardial infarction. Two-thirds of participants in both groups were vegetarian.	RCT	<p><b>Indo-Mediterranean diet group</b> (n=499): Daily targets: 250-300g fruit; 125-150g vegetables; 25-50g nuts; 400-500g whole grains, legumes, rice, maize, wheat; 3-4 servings of mustard seed oil or soy bean oil.</p> <p>As for control group: Less than 30% calories from fat, less than 10% from saturated fat, less than 300 mg/day dietary cholesterol. Advice was also given to increase physical activity, and participants were discouraged from smoking or drinking alcohol, and encouraged to do mental relaxation.</p>	Advice was given. Patients with diabetes, angina, past history of myocardial infarction, or hypertension received more frequent dietary advice than those who did not.	Less than 30% calories from fat, less than 10% from saturated fat, less than 300 mg/day dietary cholesterol. Advice was also given to increase physical activity, and participants were discouraged from smoking or drinking alcohol, and encouraged to do mental relaxation.	2 years	Food diary for 1 week completed at baseline and monthly during the intervention for the first three months, thereafter it was completed quarterly. A physical activity diary was also completed for four weeks at baseline and then monthly for the first three months; thereafter it was completed quarterly.	1. Fatal or non-fatal cardiovascular events. Other reported outcomes were: blood glucose, total, HDL, LDL cholesterol, TGs.



Reference	Population details		Study details						
	Country	Target Group	Design	Dietary intervention	Intervention delivery components	Control/ comparators	Intervention Length	Dietary assessment	Outcomes
<b>Esposito et al 2004</b>	Italy	Adult males and females diagnosed with the metabolic syndrome	RCT	<b>Mediterranean diet group</b> (n= 90): daily consumption of 400g whole grains including legumes, 250-300g fruits, 125-150g vegetables, 25-50g walnuts and increased olive oil. Nutrient targets were: 50-60% calories from carbohydrates, 15-20% calories from protein, <30% calories from fat (<10% SFA, less than 300mg cholesterol/d). As for control group: advice to increase physical activity.	Mediterranean diet group: Detailed tailored dietary advice provided, and small group sessions on calorie reduction, goal setting, self monitoring using food diaries – monthly for first year and bi-monthly for second year.  Control group: general oral and written information on food choices at baseline and subsequent visits (bimonthly sessions over the 2 years of the study) but no individualised programme.	<b>Prudent diet (control) group</b> (n=90): dietary targets were 50-60% calories from carbohydrates, 15-20% calories from protein, <30% calories from fat.  As for Mediterranean diet group: advice to increase physical activity.	24 months	Weekly? 3 day diet diaries.	Nutrient intake, endothelial function measured with L-arginine test, insulin sensitivity (HOMA), hsCRP, interleukins 6, 7 and 18.
<b>Michalson et al 2006</b>	Germany	Male and female adults with established coronary artery disease.	RCT	<b>Mediterranean diet and lifestyle group</b> (n= 48): stress management techniques and dietary targets of 5 portions/d fruit and veg (emphasis on root and green veg); > 2 portions/week fatty fish; preference for whole grain bread, pasta & rice; encouraged to consume flaxseed and walnuts; meat & sausages no > 3/week; replace beef, lamb and pork with poultry, fish or vegetarian dishes; encouraged use of olive oil, canola oil; discouraged intake of margarine apart from one commercially available olive oil based margarine; modest alcohol consumption.	<u>Mediterranean group</u> : 3 day intensive education followed by 3 hr weekly meetings for 10 weeks, then 2 hr meetings every fortnight for 9 months. <u>Control group</u> : written information only on diet and stress reduction.	<b>Written advice only group</b> (n= 53): written information with less detailed diet information including dietary principles of the Mediterranean diet and general advice on stress reduction.	12 months	7 day food diary and food frequency questionnaire at baseline and follow up. Likert scales self reported intake of olive, canola and flaxseed oil.	Heart rate, heart rate variability, systolic BP, quality of life.

Reference	Population details		Study details						
	Country	Target Group	Design	Dietary intervention	Intervention delivery components	Control/ comparators	Intervention Length	Dietary assessment	Outcomes
<b>Athyros et al 2009</b>	Greece	Adults with mild hypercholesterolaemia but no established CVD	RCT	<p>1. <b>Mediterranean diet group</b> (n=50): dietary pattern based on the Mediterranean diet score tool which favours non-refined cereals, fruits, vegetables, legumes, olive oil, fish and potatoes.</p> <p>2. <b>Plant sterol spread group</b> (n=50): AHA Step 1 hypolipidaemic diet plus 2 g/day plant stanol ester spread. The spread per 100g contained 7.1 g plant stanols as ester, 10.5g saturated fats, &lt;0.5 g trans fats, 20 g MUFA, 24 g PUFA, 800 mg vit A, 5 mg vit D and 5 mg vit E.</p>	<p><u>Mediterranean group</u>: Structured education to improve adherence to the Mediterranean diet score.</p> <p><u>Plant sterol spread / control spread groups</u>: AHA Step 1 hypolipidaemic diet advised by trained dietitians.</p>	<b>Placebo spread (control) group</b> (n=50): AHA Step 1 hypolipidaemic diet plus 2g/day of a spread that was the same as the plant sterol group was given but without plant sterols.	16 weeks (with 4 week run in)	10 point Mediterranean diet scale was administered at baseline and endpoint.	1: Change in CVD risk as assessed by: eCVD, Framingham, PROCAM & Reynolds risk equations. 2: Total chol, LDL-chol, HDL-chol, TGs, ε B, Apo serum sitost and campesterol, BP, haemostatic factors, inflammatory markers
<b>Konstantini dou et al 2010</b>	Spain	Males and females aged 20-50 years.	RCT	<p>1. <b>Traditional Mediterranean diet with virgin olive oil</b> (n=30).</p> <p>2. <b>Traditional Mediterranean diet with washed virgin olive oil</b> (n=30).</p> <p>Both groups instructed to use olive oil for cooking &amp; dressing; increase fruit, vegetables and fish; consume white meat instead of red or processed meat; prepare homemade sauce with tomato, garlic, onion, aromatic herbs, olive oil to dress vegetables, pasta, rice, &amp; other dishes; moderate consumption of red wine</p>	Personalised advice from a dietitian in a 30-minute session to each participant following the traditional Mediterranean diets, with recommendations on the desired frequency of intake of specific foods.	Control group (n=30): participants were advised by a dietitian to maintain their habitual lifestyle	3 months	FFQ, physical activity questionnaire and lifestyle questionnaire at baseline and endpoint.  Urinary excretion of tyrosol and hydroxytyrosol (major polyphenols in olive oil)	Total, HDL-, LDL-cholesterol; TGs, SBP, DBP, serum glucose

Reference	Population details		Study details						
	Country	Target Group	Design	Dietary intervention	Intervention delivery components	Control/ comparators	Intervention Length	Dietary assessment	Outcomes
<b>Estruch et al 2013</b>  <b>PREDIMED Trial</b>	Spain (11 centres)	Men aged 55 to 80 years and women aged 60 to 80 years with no CVD and with either type 2 diabetes mellitus or at least three risk factors (smoking, hypertension, elevated LDL-cholesterol, low HDL-cholesterol, overweight or obesity, family history of premature CHD)	RCT	<b>1. Mediterranean diet with extra-virgin olive oil</b> (n=2543): Target daily intake of olive oil, nuts, fresh fruit, vegetables, fish (esp fatty fish) & seafood, white meat, wine with meals (optional). Provided with extra virgin olive oil. <b>Discouraged</b> soda drinks; commercial bakery goods; sweets & pastries; spread fats; red & processed meats.  <b>2. Mediterranean diet with mixed nuts</b> (n=2454): Target daily intakes as above, foods discouraged as above. Provided with mixed nuts instead of extra virgin olive oil.	Both Mediterranean diet groups: Individual and group training sessions at baseline visit and then 3 monthly. Food provision of olive oil or nuts.  Control: Baseline dietary advice and then leaflet yearly for first 3 years, thereafter individual session followed by quarterly training sessions.	<b>Low fat diet</b> (n=2450): Target daily intake of low fat dairy; bread, potatoes, pasta & rice; fresh fruit; vegetables; lean fish and seafood. <b>Discouraged</b> vegetables oils (including olive oil), commercial bakery goods, sweets & pastries; nuts and fried snacks; red and processed meats; visible fat in meats in soups; fatty fish, seafood canned in oil; spread fats; sofrito (a sauce made with tomato & onion, and often including garlic and herbs, slowly simmered in olive oil). Provided with small non-food gifts.	Interim analyses yearly. Proposed final analysis at 6 years, trial was stopped after a median follow up of 4.8 years.	<u>All groups:</u> Baseline 14-item dietary screening tool. Annually 137-item FFQ, physical activity questionnaire. <u>Both Mediterranean diet groups:</u> 14-item dietary tool 3 monthly. Random sub-sample baseline, year 1, 3 and 5. (? 24 hr sample): Urinary hydroxytyrosol (marker of olive oil intake; n=750) plasma $\alpha$ -linolenic acid (marker of nut intake; n=375) <u>Control group:</u> 9-item dietary screening tool 3 monthly after year 3.	1: Composite of myocardial infarction, stroke, and death from CVD causes 2: Stroke, myocardial infarction, death from CVD cause, death from any cause.
<b>DASH Dietary Pattern Trials</b>									
<b>Appel et al 1997</b>  <b>Original DASH Study</b>	USA (4 centres)	Pre hypertensive adults, not on BP meds. Smokers included. Men and women, 22 years and older	RCT	<b>DASH Combination Diet</b> (n=151): Daily food based targets (Table 1.3). Moderate restriction of caffeine and alcohol. Total fat $\leq$ 27% energy, SFA $\leq$ 7% energy	Controlled Feeding, isocaloric. Lunch or dinner eaten on site, took foods for rest of day. Discretionary salt (up to 0.4g sodium), cookies or muffins provided to meet energy needs.	<b>1. Fruit &amp; Veg</b> (n=154): Daily food based targets (Table 1.3) Total fat: 37% en, SFA: 16% energy. <b>2. Typical American Diet</b> (n=154): Daily food based targets (Table 1.3) Total fat $\leq$ 37% energy, SFA $\leq$ 16% energy	8 weeks (3 week run in)	Attended on-site meals (5d per week). Participant report: discret items, if provided foods eaten. 24 hr urinary excretion of K, Mg, N, Ca, PO <sub>4</sub> , Na.	1: DBP 2: SBP SBP/DBP

Reference	Population details		Study details							Outcomes
	Country	Target Group	Design	Dietary intervention	Intervention delivery components	Control/ comparators	Intervention Length	Dietary assessment		
<b>Sacks et al 2001</b>  <b>DASH-Sodium Trial</b>	USA (4 centres)	Pre hypertensive adults, not on BP meds..  Men and women, 22 years and older.	Cross-over	<b>DASH combination diet</b> (n=208) (Table 1.3) at three different sodium levels: 1. High (72 mmol/1000 kcal) 2. Intermediate (48 mmol/kcal) 3. Low (24 mmol/1000 kcal)	Controlled isocaloric.  Feeding,	<b>Typical American diet</b> (n=204) (Table 1.3) at three different sodium levels:  1.High (72 mmol/1000 kcal) 2.Intermediate (48 mmol/kcal) 3.Low (24 mmol/1000	3 x 30 day crossover at each of three levels of sodium (2 week run in; 5 d break between each) 6 months	Daily diaries recording uneaten study foods and non-study foods eaten. Symptom/illness records.  24 hr urinary excretion of K, Na, PO <sub>4</sub> , N.	1: SBP 2: DBP	
<b>Appel et al 2003</b>  <b>PREMIER Study</b>	USA (4 centres)	Pre-hypertensive adults, not on BP meds. Smokers and people with dyslipidaemia were included.  Men and women, 25 years and older.	RCT	<b>Established plus DASH</b> (n=269): Energy restriction for weight loss (if overweight), increased physical activity, moderate alcohol restriction, reduced sodium intake, diet similar to DASH (9-12 portions fruit and veg/ day, 2-3 serves low fat dairy/ day, total fat ≤25% energy, SFA ≤7% energy.	14 group and 4 individual sessions for both the intervention and first comparator diet; second comparator diet: 1 individual session at baseline and one at follow up.  No foods provided, participants freely chose their own food.	1. <b>Established (current) recommendations</b> (n=268): Energy restriction for weight loss (if overweight), increased physical activity, reduced sodium intake, moderate alcohol restriction, total fat ≤ 30% energy, SFA ≤ 10% energy 2. <b>Advice only</b> (n=274): Printed materials, 30 min discussion re non pharmacological factors affecting BP (weight, sodium intake, physical activity, DASH diet)		24 hour recall – 2 at baseline and 2 at follow up; alcohol questionnaire; 7 day physical activity recall. Baseline and follow up: 24 hr urinary excretion of K, Na, PO <sub>4</sub> .	1: SBP 2: Hypertension status; change in DBP	
<b>Appel et al 2005</b>  <b>OmniHeart Trial</b>	USA (1 centre)	Pre hypertensive adults, not on BP or lipid lowering meds. Men and women, 30 years and older.	Cross-over (n=164)	<b>1. DASH Higher Protein:</b> carbohydrate 48% energy, protein 25% energy, total fat 27% energy. <b>2. DASH Higher Unsaturated Fat:</b> carbohydrate 48% energy, protein 15% energy, total fat 37% energy.	Controlled isocaloric  Feeding,	<b>Similar to DASH:</b> carbohydrate 58% energy, protein 15% energy, total fat 27% energy.	3 x 6 week crossover (6 day run in; 2-4 week washouts).	Daily diaries, self administered 15-item symptom checklist and physical activity questionnaire. 24 hr urinary excretion of K, Na, PO <sub>4</sub> , N.	1: SBP, LDL-cholesterol, 2: DBP, Total, HDL-chole, TGs.	

Reference	Population details		Study details						
	Country	Target Group	Design	Dietary intervention	Intervention delivery components	Control/ comparators	Intervention Length	Dietary assessment	Outcomes
<b>Blumenthal et al 2010</b>  <b>ENCORE study</b>	USA	Overweight adults aged 35 years or older with hypertension but not on BP lowering medications		<p><b>1. DASH only diet group</b> (n= 46) DASH diet as per 'combination diet' group in Appel et al 1997 (Table 1.3). Fat 27% energy (SFA 6%), Protein 18% energy. Moderate sodium restriction (RDI, 2400 mg/ 2000 kcal).</p> <p><b>2. DASH with a behavioural weight management programme</b> (n= 49) As for DASH only group but with 500 kcal/d deficit, supervised exercise sessions 3 times a week, and cognitive behaviour weight loss strategies.</p>	2 week isocaloric controlled feeding by randomised group, (except for DASH with wt management where there was an energy deficit of 500 kcal/d); both DASH groups met 4 times with nutritionist for instruction about the DASH dietary pattern. Thereafter, DASH groups: self-selected at home, weekly small group monitoring and support sessions.	<b>Usual diet control group</b> (n= 49): Asked to maintain their usual exercise and dietary habits (34% calories from fat, 15% cals from protein; calcium, magnesium, potassium, and fibre were at population 25 <sup>th</sup> centile). Weight and eating behaviour monitored twice a week.	4 months	<p>FFQ assessing previous 4 weeks and a 4 day food diary at baseline and endpoint.</p> <p>24-hr urinary sodium, potassium, calcium excretion at baseline and endpoint.</p>	<p>1: BP</p> <p>2: PWV, FMD, baroreflex sensitivity, left ventricular mass</p>
<b>Other Combination Dietary Pattern trials</b>									
<b>Takahashi et al 2006</b>	Japan	Males and females aged 40-69 years	RCT	<b>Intervention diet</b> (n= 274): Nutrient targets: reduce salt intake to <8g/d (women) or <10g/d (men); increase carotene intake to >5000ug/d; increase vit C intake to 200 mg/d. Advice to increase fruit and veg intake, reduce salted foods such as miso, vegetable pickles, salted fish and seasonings.	2 x 15 min individual dietary counselling sessions, a group lecture and 2 newsletters.	<b>Control group</b> (n=276): No intervention in the first year (provided with intervention diet in the second year).	1 year	Diet history questionnaire at baseline, and yearly. 48 hr urinary excretion of sodium and potassium	BP
<b>Nowson et al 2009</b>	Australia	Post menopausal women aged 45-75 years with high or normal BP.	RCT	<b>Vitality diet group</b> (n=): Dietary targets were 6 serves/wk lean red meat, ≥ 4 serves/d fruit, ≥ 4 serves/d vegetables, ≥ 4 teaspoons/d fats & oils; ≤ 4 serves/d whole grain breads & cereals; sodium restricted to 60-70 mmol/d.	Education provided by dietitian, then face to face contact five times after randomisation and two phone contacts (fortnightly contact by phone or face to face). <u>Vitality diet group</u> provided with portion controlled lean red meat,	<b>Reference healthy diet group</b> (n=): Unique dietary targets were ≤ 2 serves/wk lean red meat, 2 serves/d fruit, 2-3 serves/d vegetables, ≥ 8 teaspoons/d fats & oils, ≥ 4 serves/d breads & cereals (either whole grain or white), no target for sodium intake.	14 weeks (3-4 week run in)	24 hour urinary excretion of sodium, potassium, calcium, magnesium, phosphate, creatinine and urea. Daily self	Systolic BP, pulse wave analysis, pulse wave velocity, blood lipids

Reference	Population details		Study details						
	Country	Target Group	Design	Dietary intervention	Intervention delivery components	Control/ comparators	Intervention Length	Dietary assessment	Outcomes
				In common with reference healthy diet group: $\geq 3$ serves/d low fat dairy products, $\leq 4$ serves/d caffeine drinks; $\leq 2$ serves/d alcohol. Advised to use poly or monounsaturated margarines and cooking oils.	low salt bread, no added salt baked beans, salt free margarine and low salt stock powder. <u>Reference healthy diet group</u> received regular salt margarine, baked beans and canned tuna.	In common with vitality diet group: $\geq 3$ serves/d low fat dairy products, $\leq 4$ serves/d caffeine drinks; $\leq 2$ serves/d alcohol. Advised to use poly or monounsaturated margarines and cooking oils.		recording of number of serves of each food group in a diary, and a 24 hour food record was kept every fortnight.	
<b>Abedi et al 2010</b>	Iran	Post-menopausal adult women	RCT	<b>Intervention diet</b> (n=35): Five serves/day fruits and vegetables, increased whole grains, fish 2 serves/ week, SFA <10% energy, reduced salt intake.	<u>Intervention diet group</u> : 2 face-to-face and 3 lectures/group education sessions with slide demonstrations in the first month, a further face-to-face session at month 3 and monthly telephone contact.	<b>Control diet</b> (n=29): No intervention	6 months	3 x 24 hour recalls and FFQ at baseline and endpoint	Total, LDL, HDL cholesterol, TGs, SBP, DBP

## 1.6 UK dietary guidelines

Dietary guidelines in the UK are adopted by the government based on the best available scientific research, as advised the Scientific Advisory Committee on Nutrition (SACN), along with considerations of the economic context, stakeholder views including government ministers, and legislative requirements (Murphy, 2014). Prior to SACN, a similar role was performed by the Committee on Medical Aspects of Food and Nutrition Policy (COMA) (Scientific Advisory Committee on Nutrition, 2008). Dietary guidelines (Table 1.5) are communicated to the public via the 'Eatwell Plate' (Public Health England, 2014) and documented across a number of guidelines, reports and position statements. These include NICE clinical and public health guidance (National Institute for Health and Care Excellence, 2010, National Institute for Health and Care Excellence, 2006), SACN reports and position statements, and through Public Health England.

Historically, a key report was the COMA Report on Nutritional Aspects of Cardiovascular Disease (Department of Health, 1994) which proposed nutrient and dietary recommendations based on the weight of evidence, and expert opinion, at that time. These included nutrient targets for total dietary fat <35 % dietary energy, SFA <10 % energy, trans fatty acids <2 % energy, n-6 PUFA to remain stable and not increase from 6% energy with an upper limit of 10% energy, intakes of *n*-3 LCP to be increased from 0.1g to 0.2 g/day (subsequently increased by SACN to 0.45 g *n*-3 LCP/day in 2004) from oily fish, sodium intake <100 mmol/day (6 g salt/day), potassium intake >90 mmol/day (3.5 g/day) and 50 % energy from carbohydrate derived from complex carbohydrates and sugars in fruit to replace the energy deficit from fat reduction. The dietary advice was: to consume two portions of fish per week, one of which should be oily fish; to use reduced-fat spreads and dairy products instead of full-fat products; to replace fats rich in SFA with oils low in SFA and high in MUFA.

With the assistance of computer modelling, and based on average intakes from the National Food Survey, the COMA panel also presented the guidance as a dietary pattern to indicate how the advice might translate to foods in order for the general public to implement the guidelines. Recommendations from this modelling were to increase by 50% average consumption of fruit, vegetables, bread and potatoes and to increase oily fish intake to one portion a week, and to continue to substitute low and reduced fat dairy products for full fat products (Department of Health, 1994). Later quantitative recommendations to consume five portions of fruit and vegetables (400 g) a day were made by the Department of Health (Scientific Advisory Committee on Nutrition, 2008) and an increased intake of whole grain cereals was encouraged but no quantitative target set (Public Health England, 2014). Non-milk extrinsic sugars (NMES), (which will in future be referred to as 'free sugars' in line with the SACN draft recommendations for carbohydrate intakes) are recommended at intakes of less than 11% total energy intake (Scientific Advisory Committee on Nutrition, 2008) (which in the future will be amended to less than 10% of total energy as 'free sugars') (Scientific Advisory Committee on Nutrition, 2014).

Table 1.5 Summary of current UK dietary guidelines

Summary of current UK recommendations	
Total fat	≤ 35 % energy
Saturated fat	< 11 % energy
Salt	< 6 g/day
Fruit & vegetables	≥5 x 80g portions/day
Oily fish	At least 1 x 140g portions/week
Whole grains	Eat where possible
Non starch polysaccharides	18 g/day
Total sugars	-
Non milk extrinsic sugars	≤ 11 % energy

Dietary guidelines are promoted to the whole population to reduce risk of chronic disease, including cardiovascular disease. In the UK, it has been estimated that 30–35 000 deaths could be avoided if all dietary recommendations were adhered to by the population (Scarborough et al. 2010). However several studies across a number of countries have noted disappointingly poor adherence to dietary guidelines for the majority of the population (Murphy, 2014, Bates, 2012, Srinivasan, 2013, Haack and Byker, 2014, Australian Bureau of Statistics, 1999). Factors influencing the uptake of dietary guidelines are known to be complex and, despite a general lack of coherent enquiry in the literature, are likely to be multifactorial across individual (Desroches et al., 2013, Bautista-Castano et al., 2004, Zazpe et al., 2010), social (Koikkalainen et al., 1996, Khan, 1981, Robinson et al., 2013) and environmental influences (Lappalainen et al., 1997, Khan, 1981, Cohen and Babey, 2012, de Vet et al., 2011).

## 1.7 Achieving dietary change

A wide range of strategies have been used to support behaviour change in intervention studies. Dietary interventions delivered in the research setting and clinical practice vary in the number of behaviours targeted and the strategies adopted - ranging from written information only to 'multiple component' interventions incorporating written, verbal and technological methods to provide a tailored intervention for the individual (Artinian et al., 2010). Written advice is typically designed to meet the needs of the generic participant or patient and is not individualised. This strategy is effectively a form of self-help intervention, and indeed is often adopted for control and comparator groups in dietary intervention studies. In general, the use of brochures and pamphlets in the absence of supporting strategies such as verbal counseling and goal setting are largely considered to be ineffective (Yanek et al., 2001, Whitt-Glover et al., 2013).

More effective are the use of group, individual and multi-component strategies (Artinian et al., 2010). Group-based interventions provide social support and role modeling opportunities as inherent features that may help individuals to make dietary changes (Wing and Jeffery, 1999,



Murray et al., 2013, Murray et al., 2012) and have been used previously in randomised controlled trials of lifestyle interventions to modify cardiovascular risk (Appel et al., 2003, Aldana et al., 2006). Individually focused interventions are more common in randomised controlled trials as well as being used extensively in clinical practice. They involve some degree of tailoring of an intervention, which considers individual factors relating to lifestyle, resources and preferences (Beck et al., 2010) as well as support in problem solving (Lindström et al., 2003). Tools used in individual interventions include face-to-face communication, telephone, electronic and combined approaches. Combined approaches are considered most successful in facilitating dietary change (Artinian et al., 2010, Desroches et al., 2013).

Cognitive-behavioural strategies are often considered an essential component of any dietary change intervention, and encompass goal setting, self-monitoring, frequent and prolonged contact, feedback and reinforcement, and incentives. Incorporating two or more such strategies has been linked to greater success (Artinian et al., 2010). Goals that focus on concrete behaviours (such as increasing fruit and vegetables) rather than clinical endpoints (eg blood cholesterol levels) are considered more useful, as they are controlled directly by the individual. Self monitoring enables ongoing feedback which reinforces the behaviour each time it is performed (Strecher et al., 1995, Artinian et al., 2010, Cullen et al., 2001).

In terms of research studies, protocols incorporating scheduled follow up sessions have been found to be more effective, including face-to-face, telephone or email follow up (Artinian et al., 2010). Regular feedback and reinforcement, a feature of scheduled follow up, is also a frequent characteristic of successful interventions and can be a strong motivator of dietary and physical activity behavior change (Eakin et al., 2007, Yanek et al., 2001, Fries et al., 2005). In addition, incentives (particularly financial incentives in workplace interventions) have been highlighted as a motivating factor and although there is limited evidence, non-financial incentives (such as a small refrigerator magnet) may also be worthwhile (Campbell et al., 1999).

The adoption and maintenance of health promoting dietary habits is known to be challenging (Artinian et al., 2010, Murray et al., 2013, Murray et al., 2012) relying on more than just knowledge. Behaviour change models underpin nutrition counseling, and practitioners use them as frameworks to identify internal and external issues along with the dynamics of behaviour change for individual clients (Spahn et al., 2010).

A comprehensive model for behaviour change has been developed, known as the 'behaviour change wheel' (Michie et al., 2011), which characterises interventions through an interplay of multi-level factors: sources of behaviour (capability, opportunity and motivation), intervention functions (restrictions, education, persuasion, incentivisation, coercion, training, enablement, modeling and environmental restructuring) and policies (fiscal measures, guidelines, environmental and social planning, communication and marketing, legislation, service provision and regulation). This model attempts to capture the many factors that underpin individual behavior change, but in reality the ability of an individual to manipulate many of these variables is limited. Public health programmes, which are targeted at a population level, may be more amenable to cross-sector working to address the policy level aspects of behavior change.

## **1.8 Translating and implementing evidence for cardiovascular disease prevention**

Studies investigating the implementation of evidence-based dietary interventions into real world settings have consistently shown more modest effects than the efficacy studies they were based on (Davey Smith and Ebrahim, 1998, Tang et al., 1998, Artinian et al., 2010, Rothman, 2000, Brunner et al., 1997, Appel et al., 2003). Implementation research, often categorised together with 'translational research', aims to address the often slow and unpredictable uptake of research findings into health care practice (Eccles et al., 2009). It is multidirectional and concerned with the integration of basic, patient and population based research with the longer-term aim of improving public health (Rubio et al., 2010). The call for a greater focus on "real world" effectiveness trials as imperative adjuncts to efficacy trials is not new (Glasgow et al., 2003, Haynes, 1999) and has become an increasingly important priority over the last five years (Public Health England, 2010, Eccles et al., 2009, Cooksey, 2006, Soderquest and Lord, 2010, Snape et al., 2008).

Understanding how an intervention works is essential to designing more effective public health programmes and the implementation of evidence based interventions across different groups and settings (Craig et al., 2006). In addition to the effect on the outcomes measured, translation of trial interventions into practice requires information about the details of, and evidence supporting, the intervention, the population targeted, the context in which the intervention was studied, and the involvement of participants in the evaluation (Tripp-Reimer and Doebbeling, 2004). 'Process evaluation' is an essential component of translational research and is concerned with a number of factors associated with implementation, including participant satisfaction, delivery (how the activities associated with the intervention were delivered), intervention fidelity (materials and delivery), and contextual aspects (aspects of the environment that influence the implementation). (Hughes and Margetts, 2010). The intervention should be reproducible, with all components reported to enable implementation outside of the study (Hoffmann et al., 2014).

Identifying barriers and enablers to participation and compliance is an important component of process evaluation. In terms of compliance to dietary guidelines, barriers previously identified include the social, eating and policy environment (Story et al., 2008, Artinian et al., 2010); family, individual and culture-based food preferences and preparation methods; lack of individual readiness to change, and the high cost (or perceived high cost) of food (Rowe et al., 2011). It is recognised that interventions that have multiple components, are culturally sensitive and delivered in settings appropriate to the population targeted, account for literacy levels and barriers to dietary change are most likely to be effective for CVD prevention (Artinian et al., 2010).

## **1.9 Summary**

Primary prevention of CVD has traditionally been directed at high-risk individuals (Emberson et al., 2004) whereas in fact most CVD occurs in individuals at average risk (Rose, 1985, Collins and Altman, 2012, Strachan and Rose, 1991). The recent JBS3 guidelines and risk calculator for

the first time spell out the need to shift the focus beyond individuals who are at immediate risk, and focus prevention on those who are at longer term risk (JBS3, 2014) and where lifestyle interventions can be effective.

Although not without controversy, there is a vast array of evidence supporting dietary change for the prevention of CVD. Dietary patterns characterised by high intakes of fruits, vegetables, whole grains, nuts, legumes, unsaturated oils, low-fat dairy, poultry, and fish; low intakes of red and processed meat, high-fat dairy, and sugar-sweetened foods and drinks; and a moderate intake of alcohol have been demonstrated to reduce both CVD risk factors in high risk populations and clinical endpoints in ecological studies of populations (United States Department of Agriculture, 2014).

Government endorsed dietary guidelines, supported by such evidence, are directed at reducing chronic disease including CVD in the general population rather than those deemed at high risk. Evidence for the efficacy of dietary interventions and lifestyle change in populations at average, rather than high, risk is needed to provide cost-effective alternatives to medication. It is therefore important to demonstrate the efficacy of the current UK dietary guidelines, and to consider their translation and implementation beyond the trial setting to inform public health initiatives for CVD prevention.

## **1.10 Hypotheses**

The primary hypothesis being tested is:

An integrated dietary approach modifying the overall dietary pattern to conform with UK dietary guidelines for the prevention of CVD (5 portions of fruit and vegetables per day, increased consumption of whole grain cereals and oily fish; moderate total fat and reduced saturated fat, added sugars and salt intake) for a minimum of 12 weeks will lead to significant reductions in daytime systolic BP, a reduction in TC:HDL-C, and improvements in endothelial function compared to a conventional UK diet in healthy adults aged 40 to 70 years.

In a secondary study the following hypothesis will be tested:

A cardioprotective dietary pattern (cardioprotective diet) will not be more expensive than a dietary pattern representative of many adults in the UK (conventional UK diet).

## **1.11 Objectives**

This thesis will explore whether an overall dietary pattern consistent with UK dietary guidelines over a twelve week period is associated with improvements in cardiovascular risk in people aged 40-70 years, when compared with a conventional UK diet. An investigation into the affordability of a cardioprotective diet, compared with a control diet, will be made, and robust qualitative methodology will be used to identify self reported barriers and enablers to compliance with dietary change, which will inform the translation and implementation of the results to clinical and public health practice.

There are three objectives:

1. To develop, deliver and evaluate in a randomised controlled trial a cardioprotective dietary intervention based on the UK dietary guidelines and using an integrated dietary approach, for comparison with a conventional UK diet in free living men and women aged 40-70 years. (Chapter 3)
2. To conduct a qualitative study to understand the experience of undergoing dietary change and identify factors relating to compliance to the dietary intervention using semi-structured interviews. (Chapter 4)
3. To undertake a costing analysis study to determine if a self-selected cardioprotective diet based on UK dietary guidelines is more expensive than a conventional UK diet. (Chapter 5)

## Chapter 2 Main Methods

### 2.1 Introduction

This chapter describes the rationale and main methodological techniques used within this thesis. Not all studies used all techniques, and detailed methods for each study will be provided in the relevant chapter.

A summary of the methods used for each of the three studies comprising this thesis is presented in Figure 2.1.

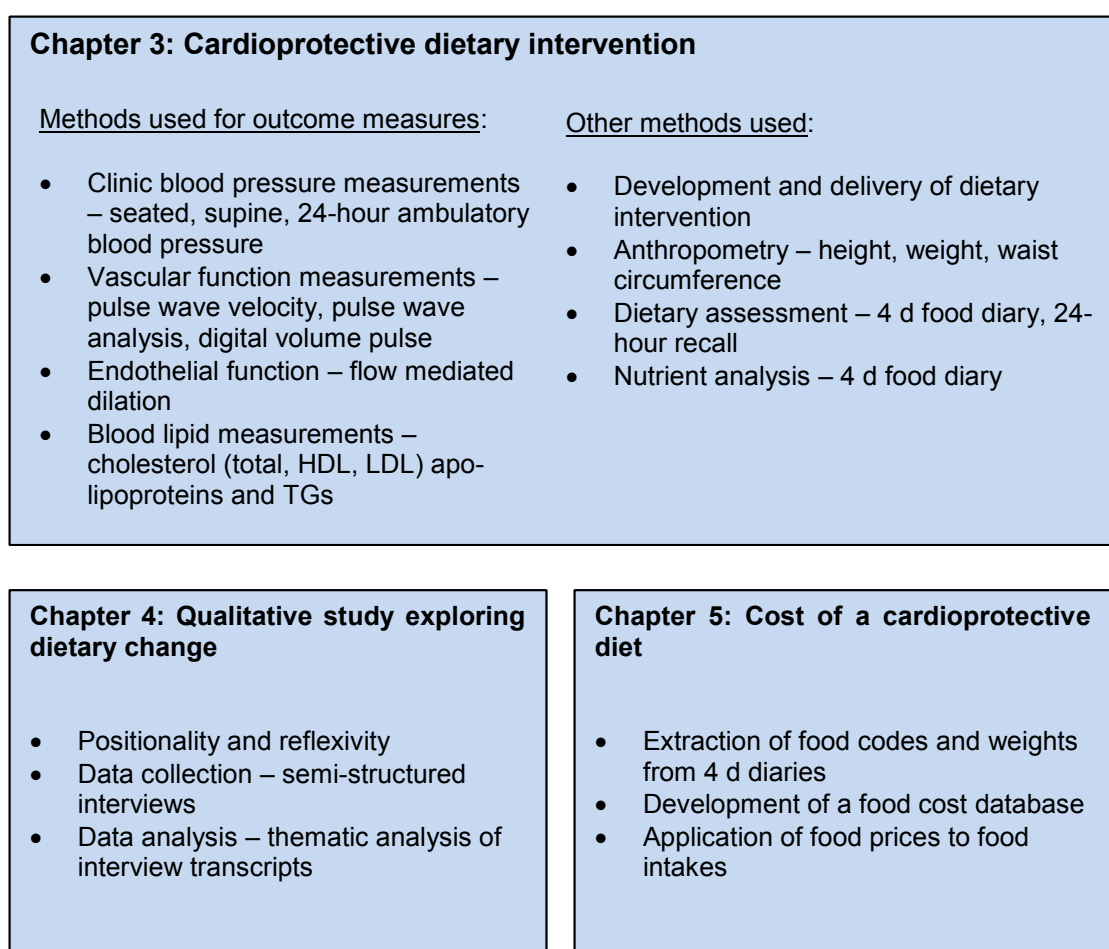


Figure 2.1 Overview of methods used in the three studies

### 2.2 Development of a cardioprotective dietary intervention

#### 2.2.1 Dietary targets

The protocol for the study, developed in collaboration with the Food Standards Agency, specified that the cardioprotective diet should supply SFAs at around 10 % of energy, 16 % of energy as MUFAs, 6 % of energy as PUFAs and <1 % of energy as *trans* fatty acids; restriction on salt intake to <6 g/day; five portions of fruit and vegetables/day (two portions in exchange for snack foods); two portions of fish a week (one of which should be oily to provide 3.2 g *n*-3 LCP/week);

whole grain cereal intake to account for >50 % cereal intake and restrictions on intake of added sugars. The diet was designed to be isocaloric with no intentional target for energy reduction.

## **2.2.2 Identification of foods suitable for dietary manipulation**

The implementation of these dietary goals, to form a dietary intervention that could be easily adopted by participants randomised to the cardioprotective diet arm, was undertaken using data available on food selection and preferences in the UK adult population. Firstly, the (2008-09 Rolling Survey) National Diet and Nutrition Survey (NDNS) results were explored to identify foods from each food group that are more frequently consumed by UK adults aged 40 to 70 years (Bates et al., 2009). As this age range straddles two of the age categories used by the NDNS (which stratifies populations into 19-64 year olds, and those aged over 65 years), food intake from both of these age categories was scrutinised (Table 2.1). Foods that were consumed by 45% or more of the population in either or both of the age groups were specifically targeted, as these were considered important foods requiring manipulation to achieve the dietary targets. Other foods identified as important related directly to the dietary targets (eg fish and oily fish, reducing salt and added sugars) or were suitable substitutes for commonly consumed foods (eg reduced fat yoghurt as a replacement for cream and ice cream, nuts as a replacement for crisps).

## **2.2.3 Dietary modelling**

For the cardioprotective group, dietary modelling was undertaken to ensure the intervention was isocaloric (Table 2.2) by estimating the kilocalorie change to the diet as a result of key food exchanges advised, based on average intakes reported in the NDNS (Public Health England and Food Standards Agency, 2014). No advice was given to restrict the intake of food energy, and fruit was encouraged in place of crisps, biscuits, cakes and buns; in addition snacks were provided (portion of nuts and a wholegrain cereal nut bar per day) to offset the expected reduction in energy as a result of recommended dietary changes.

To avoid the potential for bias and prevent possible weight gain in the control group, snack foods were also provided to these participants (Kit Kat 2 finger bar, crackers), although these were encouraged as occasional foods rather than as a recommended daily requirement. If weight gain of more than 1kg was detected during the study, participants were advised to reduce snacking including the study snack foods provided. To achieve the targets for fat in both the cardioprotective and control groups, specially manufactured oils and spreads were provided and a food exchange model, similar to that previously used in the RISCK and LIPGENE studies, was used to swap the manufactured products for cooking oils and spreads usually consumed (Shaw et al., 2009, Moore et al., 2009). Participants were instructed to consume a minimum amount (2-4 teaspoons of spread and 1-2 tablespoons of oil) each day during the dietary intervention period. Study snack foods (unroasted, unsalted macadamia nuts or almonds, and a wholegrain nut cereal bar) for the cardioprotective diet group were chosen to be high in MUFAs, as previous intervention studies have achieved lower than expected intakes of MUFAs using a similar exchange model (Nydahl et al., 2003, Shaw et al., 2009).

Table 2.1 Rationale for targeting of and strategies adopted for dietary manipulation of food groups for cardioprotective dietary intervention

Food group	Potential for dietary manipulation	Strategies adopted
<b>Foods selected because they are consumed by <math>\geq 45\%</math> of population aged 19-64 years or 65 years and over (Bates et al., 2009)</b>		
Pasta, rice and other miscellaneous cereals	Increase intake of whole grain cereals	<ul style="list-style-type: none"> <li>Written and verbal advice to replace white pasta and rice with wholegrain varieties</li> <li>Provision of wholegrain pasta and rice as pantry items</li> </ul>
Bread, white	Increase intake of whole grain cereals, reduce salt intake.	<ul style="list-style-type: none"> <li>Written and verbal advice to replace white bread with wholegrain varieties, and to limit intake to 2-4 slices bread per day.</li> <li>Recipe for salt free bread provided.</li> </ul>
Breakfast cereal, high fibre	Reduce salt and added sugar intake, increase intake of whole grain cereals, reduce refined cereal intake	<ul style="list-style-type: none"> <li>Written and verbal advice to choose only from the four breakfast cereals provided</li> <li>Provision of jumbo rolled oats, Shredded Wheat, Oatibix, muesli (untoasted, no added sugar or salt) as pantry items.</li> </ul>
Biscuits	Reduce salt and added sugar intake, increase intake of whole grains, reduce intake of saturated and trans fatty acids, reduce total fat intake	<ul style="list-style-type: none"> <li>Written and verbal advice to limit or avoid these foods, apart from whole grain crisp breads with less than 500mg/100g salt, whole grain cereal bars with nuts with no added salt and minimal added sugar (less than two teaspoonfuls or 8g per serving).</li> <li>Provision of whole grain cereal bars (maximum one 45g bar per day) as replacement snack for biscuits, buns, cakes, pastries and fruit pies</li> </ul>
Buns, cakes, pastries and fruit pies		
Milk, semi-skimmed	Reduce saturated fat intake	<ul style="list-style-type: none"> <li>Written and verbal advice to substitute semi-skimmed milk for skimmed or 1% fat milk</li> </ul>
Cheese	Reduce saturated fat intake, reduce salt intake	<ul style="list-style-type: none"> <li>Written and verbal advice to keep portions small (30g) and restrict intake to no more than three times per week; and encourage options with a lower fat and salt content.</li> </ul>

Food group	Potential for dietary manipulation	Strategies adopted
Eggs and egg dishes	Reduce saturated fat intake	<ul style="list-style-type: none"> <li>Verbal advice to consume a maximum of three eggs per week</li> </ul>
Butter	Reduce saturated fat intake, replace saturated fat sources with polyunsaturated and monounsaturated fats	<ul style="list-style-type: none"> <li>Written and verbal advice to avoid butter and to instead use only the study spread provided, 2-4 teaspoons per day</li> <li>Provision of study spread containing per 100g: 19g saturated fatty acids, 20g polyunsaturated and 61g monounsaturated fatty acids.</li> </ul>
Polyunsaturated spread (41-75% fat)		
Bacon and ham	Reduce salt intake	<ul style="list-style-type: none"> <li>Avoid ham and bacon products. Suggestions to replace included freshly cooked sliced meats (leftover roast meat, skinless chicken) or the provided tins of oily fish.</li> </ul>
Beef, veal and dishes	Reduce saturated fat intake, increase fish and vegetable intake	<ul style="list-style-type: none"> <li>Include meat and chicken up to three times per week.</li> <li>Written and verbal advice to choose lean cuts, remove all visible fat, to remove the skin of poultry before eating, limit portion size and restrict to a maximum of three times per week including chicken; include two or more portions of fish each week, and include beans and pulses in place of meat.</li> </ul>
Chicken, turkey and dishes		
Vegetables and potatoes	Increase portions of vegetables consumed each day, reduce saturated fat and salt	<ul style="list-style-type: none"> <li>Aim to include at least 2-3 portions of vegetables each day, with advice to increase serving size to approx. 80g</li> <li>No specific advice on potato, other than to discourage potato products with added fats and salt (but jacket potato used as an example of a lower salt alternative to bread)</li> </ul>
Crisps and savoury snacks	Reduce sources of saturated fat and salt, increase portions of fruit consumed each day, increase whole grains	<ul style="list-style-type: none"> <li>Limit intake and choose healthier alternatives</li> <li>Snacks based on nuts, whole grains, fresh fruit, vegetables and low fat dairy products can be included daily</li> <li>Provision of single serve (10-15g) packets of whole, unroasted and unsalted almonds and macadamia nuts.</li> </ul>
Fruit	Increase portions of fruit consumed	<ul style="list-style-type: none"> <li>Aim to include at least 2-3 portions of fruit each day.</li> </ul>



Food group	Potential for dietary manipulation	Strategies adopted
	each day, replace less healthy snacks (higher in sugar/ salt/ saturated fat) with fruit	<ul style="list-style-type: none"> <li>• Advice to consume fresh fruit with guidance on serving size of approx. 80g. Smaller portions of dried fruit advised.</li> <li>• Replace less healthy snacks with fresh fruit.</li> </ul>
Sugars, including table sugar	Reduce added sugars	<ul style="list-style-type: none"> <li>• Limit added sugar in tea and coffee to a maximum of 4 teaspoons per day. Use sweeteners or sugar alternatives in place of sugar.</li> <li>• Limit fruit juice to one small glass per day.</li> <li>• Provision of wholegrain breakfast cereals with no added sugar</li> <li>• Choose low fat yoghurts and custard with minimal added sugars</li> <li>• Limit chocolate, sweets, biscuits and cakes.</li> </ul>
Soft drinks, not low calorie	Reduce added sugars	<ul style="list-style-type: none"> <li>• Avoid all fizzy drinks, squashes, juice drinks, energy drinks as they contain a lot of sugar. Low sugar ('diet' or 'Lite' versions) of these drinks can be included.</li> </ul>
Tea, coffee and water	Reduce added sugars, saturated fat.	<ul style="list-style-type: none"> <li>• Tea and coffee are allowed, include other drinks as well</li> <li>• Use skimmed milk particularly in drinks with large amounts of milk such as cappuccinos and lattes</li> <li>• Limit sugar in tea and coffee to no more than 4 teaspoons per day in total, use sugar alternatives/ sweeteners to replace sugar</li> <li>• Enjoy water as a drink, add a slice of lemon or lime for flavour.</li> </ul>
Savoury sauces, pickles, gravies and condiments	Reduce salt intake, reduce intake of added sugars.	<ul style="list-style-type: none"> <li>• These are often high in salt and/or sugar</li> <li>• Homemade sauces and stocks are preferable if you have time</li> <li>• Commercial gravy powders and granules can be very high in salt and should be avoided or limited to a small portion eg 2-3 tablespoons per serve</li> <li>• Choose commercial sauces with reduced sugar and salt.</li> </ul>

Food group	Potential for dietary manipulation	Strategies adopted
		<ul style="list-style-type: none"> <li>Provision of reduced sugar and salt ketchup and brown sauce.</li> </ul>
<b>Foods selected as directly related to dietary targets (Bates et al., 2009)</b>		
Cooking oil	Maintain fat intake at around 35% energy, increase the proportion of monounsaturated and polyunsaturated fats, reduce proportion of saturated fats, maintain energy intake (weight maintenance).	<ul style="list-style-type: none"> <li>Provision of study oil (high oleic sunflower oil) containing per 100g: 9g saturated fatty acids, 10g PUFAs, and 80g monounsaturated fatty acids</li> <li>Advice to include 1-2 tablespoons of oil each day</li> </ul>
Oily fish	Increase portions of oily fish consumed regularly	<ul style="list-style-type: none"> <li>Provision of tinned oily fish (no added salt). Reimbursement of fresh oily fish, limited to 1-2 portions per week</li> </ul>

Table 2.2 Isocaloric modelling for cardioprotective dietary intervention

Recommendation	Estimated kcal/day - recommendation	Basis for estimate	Food being replaced	Estimated kcal/day for food being replaced	Basis for estimate	Net difference (kcal/day)
Choose 1% fat or skimmed milk	<b>111</b>	300 ml/day, average of 1% and skimmed milk	Whole or semi-skimmed milk	<b>169</b>	300 ml/day, average of whole and semi-skimmed milk	<b>-58</b>
Cheese, reduce to no > 90g/week & choose lower fat/salt where possible	<b>51</b>	15g/day Edam cheese	Cheddar cheese,	<b>83</b>	20g/day Cheddar cheese	<b>-32</b>
Fruit in place of biscuits, cakes, buns	<b>41</b>	Medium sized pear	Biscuit, cakes, buns	<b>169</b>	41g/day, average of chocolate digestives, Madeira cake, Chelsea bun	<b>-128</b>
Fruit in place of crisps	<b>47</b>	Medium sized apple	Crisps	<b>65</b>	12g/day plain crisps	<b>-18</b>
Avoid deep fried chips, choose oven chips or jacket potato in place of	<b>100</b>	Mean of oven chips (65g/day) and jacket potato (70g/day)	Chips	<b>155</b>	65g/day chips, retail, fried in vegetable oil	<b>-55</b>
Nuts, unsalted/unroasted	<b>82</b>	Mean of macadamia nuts (10g/day) and almonds (15g/day)	N/A	-	N/A	<b>+82</b>
Wholegrain nut cereal bar (45g/day)	<b>245</b>	45g bar/day	N/A	-	N/A	<b>+245</b>
<b>Total daily energy difference</b>						<b>+36 kcal/day</b>

## 2.3 Dietary Assessment Methods

Dietary assessment methods aim to identify the type, amount and frequency of habitual food intake of an individual. Methods vary, and can be prospective or retrospective. Assessment of food intake involves the identification of all the food and drink, along with the many different variations of these (such as brand, portion, processing and cooking method used), consumed by an individual. All of these variables introduce potential sources of error, and therefore a greater amount of data is required (than would be needed for a less variable measure) to ensure the results are reliable (MacIntyre, 2009). Food intake assessment methods are also known to have large intra-individual variations and isolated assessments are weak predictors of habitual dietary intake (Buzzard, 1998) and there is no method for assessing dietary intake in free-living individuals that is not without error. In addition, underreporting of intakes occurs in most dietary assessment methods resulting in systematic bias (Freedman et al., 2006).

Direct measures of food intake are commonly used in dietary intervention studies. Direct measures include food records for specified days (weighed or estimated food diaries - usually of less than or equal to 7 days' duration, and 24-hour recalls) and reports of food intake (food frequency questionnaires or diet histories over longer periods ie up to 12 months) over a specified time period (MacIntyre, 2009, Black and Cole, 2001). Previously, weighed food records kept over a 7-day period were considered the 'gold standard' method of dietary assessment, however a better understanding of the limitations of this method (Livingstone et al., 1992) has meant that a combined approach using dietary records alongside more objective biomarkers is considered necessary (Bingham et al., 1995). Determining nutrient intakes from individuals involves firstly determining all the food and drink consumed, along with the frequency, with sufficient detail to select appropriate portion size and food items from standard food tables. The nutrient intake can then be calculated by multiplying the portion size in grams by the frequency and the nutrient content per gram (MacIntyre, 2009).

Weighed food records are a prospective method of dietary assessment requiring participants to weigh and record each item of food and drink as they are consumed. The approach is detailed, and requires brand names, methods of preparation, recipes and the weight of any leftovers to be recorded. All details are recorded in a purpose-designed diary provided to participants, along with a set of weighing scales. Additional information such as the time and place that the food or drink was consumed, and whom it was consumed with, may also be recorded. Weighed records are typically kept for 3, 4, 5 or 7 consecutive days, including at least one weekend day to represent habitual intake.

The main advantage to weighed records is the precise nature of the portion size and details of the food consumed, the additional information on food habits (such as frequency and timing of meals) it provides, and (if completed as instructed ie at the time food is consumed) the fact that the method does not rely on memory. The main disadvantage is the high burden on participants, who must be both trained and motivated to follow the strict process of recording food intake and there is evidence that motivation reduces the longer the record is kept (Livingstone et al., 1992). The method is time consuming for both participants and researchers, and some participants may

change what they eat and drink in an effort to reduce the burden (Rebro et al., 1998).

Estimated food records have been found to approach the level of accuracy of weighed records (Bingham et al., 1995). They are less onerous and are collected using very similar methods, however instead of weighing all foods the portion sizes consumed are estimated using common household measures (eg cups, teaspoons) or photographs to assist with quantification. The descriptive portion sizes are then converted to weight by the researcher for analysis of nutrient intake. Participants still require training to ensure they correctly record all foods and drinks, including reliable information on brands, cooking methods and portion size. Although participant burden is reduced when compared to weighed records, accuracy is improved if food and drink is recorded as and when it is consumed which can lead to the individual varying their intake from their usual diet. For both weighed and estimated food records, the day to day variation in intake will be a source of error – increasing the number of days recorded will reduce the error, however the quality of the record declines as the number of days increases (Gersovitz et al., 1978).

Dietary recall methods are retrospective, usually provided through a face-to-face or telephone interview, or sometimes through a written questionnaire that is self-completed. Twenty-four hour recalls are most common and usually involve the participant recalling all food and drink eaten in the past 24 hours, considered to be the most reliable period for recall. Periods longer than 24 hours are considered to be subject to recall bias and memory limitations (MacIntyre, 2009). Interview techniques used in the recall can improve the quality of the data, and help to overcome the problem of poor memory of what was consumed by the individual. The 'multiple pass' recall method involves the interviewer asking the participant to recall food items (focusing on different aspects) three to five times to ensure all items of food and drink consumed are remembered. Protocols differ between studies for multiple pass recalls, however all tend to allow free and uninterrupted recall followed by probing questions to clarify intake (including portion size) and concluding with a review of what was recalled and often the time or location of consumption (Medical Research Council).

Multiple pass recalls are more acceptable to participants than weighed prospective record methods (Holmes et al., 2008) and the multiple pass method has been shown to improve the accuracy of recall in both men and women (Conway et al., 2004, Conway et al., 2003). Food models, photographs and household measures can be used to better quantify portion sizes of foods eaten. The main strengths of this method are the reduced burden, and no literacy requirement for the participant. As well as the reliance on the participant's memory to recall all foods and drinks consumed, a major limitation of the 24 hour recall is that it does not account for day-to-day variation in intake - although a single recall is sufficient for large studies where it is useful as a measure of the group's average dietary intake (MacIntyre, 2009, Block, 1982).

## **2.4 Methods of dietary assessment used in cardioprotective dietary study**

### **2.4.1 Food diaries**

Participants completed 4-day food diaries just prior to the vascular visits at baseline (Week 0) and endpoint (Week 12). Prior to the baseline vascular visit, participants were provided with a food diary (purchased from the Medical Research Council Human Nutrition Research unit) and given instructions on how to complete a 4-day estimated food record accurately. Diaries were completed on agreed dates from Sunday to Wednesday or Wednesday to Saturday, thus ensuring one weekend day was included in the record. The diary included photographs to represent small, medium and large portion sizes for common foods (Nelson et al., 1997) and participants were asked to indicate which of the photographs best represented the portion size eaten, or to use household measures, or packet sizes of food items to estimate portion. Participants were specifically asked not to change what they normally ate or drank, and to record every item of food or drink as soon as possible after consuming them. The diary was divided into four time slots for each day: early morning (06.00-09.00), morning (09.00-12.00), early afternoon (12.00-14.00), afternoon (14.00-17.00), early evening (17.00-20.00), evening (20.00-22.00), overnight (22.00-06.00) and included a space to write recipes for foods prepared at home on each day. Participants were encouraged to provide labels of foods eaten over the four days, and to carry the diary with them over the four days so that food could be recorded at the time of consumption (and reduce reliance on memory of what was eaten).

A baseline assessment of participants' usual diets were assessed using the food diaries completed at baseline and repeated after 12 weeks to assess compliance to the intervention. Each food diary was reviewed for completeness by either the study dietitian (baseline diaries) or a trained researcher experienced in food diary methodology (endpoint diaries; the discrepancy due to the dietitian being engaged in mid point visits for other participants), and missing or incomplete food descriptions, recipes and portion sizes were identified and clarified directly with the participant.

### **2.4.2 24-hour recalls**

Dietary intakes were assessed twice by the study dietitian during the intervention via a triple-pass 24-hour recall protocol, using the method described in the Low Income Diet and Nutrition Survey (Holmes et al., 2008). The primary purpose was to assess compliance and provide a basis for reinforcement of dietary advice consistent with the intervention the participant was randomised to. The first recall was face-to-face and undertaken four weeks after baseline; the second recall interview was by telephone and was undertaken eight weeks after the baseline visit. The three passes were undertaken using the same order for each participant across both recalls. The first pass was a free and uninterrupted recall by the participant of all food and drink consumed the previous day. Time of consumption was recorded, recipes were obtained and portion sizes were estimated during the second pass of each recall. In the first recall (face-to-face interview) this

was done using food photographs (Nelson et al., 1997) and either household measures, package sizes or the portion sizes from the first recall were used as a basis for quantifying those in the second recall (telephone interview). The third pass involved the researcher reciting back the recall as determined by the first and second passes, concluding with a checklist of foods to ensure no commonly consumed foods, including those provided as part of the study, had been forgotten in the recall.

### **2.4.3 Nutrient analysis**

Nutrient intakes were calculated from the 4-day dietary records using NetWisp (version 3.0; Tinuviel Software, UK) which uses nutrient information taken from the UK Nutrient Databank (McCance and Widdowson Composition of Foods Integrated Dataset incorporating The Composition of Foods, 6<sup>th</sup> edition (Food Standards Agency, 2002) plus published supplements and the earlier 5<sup>th</sup> edition (Chan et al., 1996, Ministry of Agriculture Fisheries and Food, 1998, Chan et al., 1995, Chan et al., 1994, Holland et al., 1993, Holland et al., 1992a, Holland et al., 1992b, Holland et al., 1991, Holland et al., 1989, Holland et al., 1988, Tan et al., 1985) using the machine-readable format supplied under licence by the Office of Public Sector Information.

Portion sizes were converted to weights based on the information in each diary. Where the participant had used the portion size photographs in the diary, standard portions were assigned according to which photograph was chosen. Where household measures or whole units were used, the portion size was estimated using a food portion size reference book based on UK food portion sizes (Food Standards Agency, 1994). The food and drink from each diary was matched to the code of an appropriate food in the Databank at the time of input into NetWisp. Where there was no food in the databank to approximate the food reported in the diary, a new food code was made by copying the most similar food code available and updating it with nutrient data from packaging supplied with the diary or from a similar product. Where reported in the diary, nutrient content of recipes were calculated by entering a code for each of the ingredients and the weight of each in grams. Weight loss on cooking was estimated by applying the weight loss for a similar standard recipe as reported in the appendix to the standard food tables (Food Standards Agency, 2002). Once entered, each recipe was designated a new food code. Where there was no recipe recorded in the diary, a standard recipe was used from a cookery text book (Foskett et al., 2004) or the BBC Good Food website (BBC Good Food, 2013).

Each diary was rated using a three-point scale according to degree of completeness. Where the diary was fully completed (all food items able to be fully identified, portion sizes clearly reported, recipes and labels provided) it was rated a '3', where there was insufficient information provided in the diary (clear under-reporting, lack of detail for foods and drinks consumed and/or portion sizes) it was rated a '1'. Diaries which were adequately recorded with some details omitted or unclear were rated a '2'. In addition, basal metabolic rate (BMR) was calculated for each individual using the Schofield equation (Schofield, 1985) and underreporting was identified in participants whose diaries reported energy intake less than 1.2 times BMR (McCrory et al., 2002).

## 2.4.4 Biomarkers of dietary intake

A number of objective biomarkers of nutritional intake were measured as part of the larger cardioprotective dietary intervention study, but were not the focus of this thesis. Table 2.3 summarises the biomarkers measured; for completeness, the methods for these have been included in Appendix 2.1 Biomarkers of dietary intake

Table 2.3 Summary of biomarkers used as objective measures of target foods and nutrients

Food/ nutrient	Biomarker used in cardioprotective dietary study
Salt	Urinary sodium
Fruit and vegetables	Urinary potassium
Added sugars	Urinary sucrose and fructose
Whole grains	Serum alkylresorcinol Serum folate
Oily Fish	Total erythrocyte phospholipid fatty acid composition ( <i>n</i> -3 LCP)

## 2.5 Measures of cardiovascular risk

### 2.5.1 Blood pressure

Blood pressure is highly variable within individuals and is influenced by many factors, including the environmental conditions of the measurement itself. The variability of BP leads to greater errors with single measurements, and the phenomena of ‘white coat’ hypertension (the elevation of ambulatory BP in normotensive individuals in the clinic setting, sometimes by up to 30 mmHg) (O'Brien et al., 2003). Methods of measurement include clinic BP monitoring (using standardised protocols that limit the impact of environmental factors with at least two measurements taken) and ambulatory BP monitoring (periodic monitoring of BP over a number of hours to provide a BP profile using multiple readings). Ambulatory BP (ABP) is considered superior to other measures of BP, due to its steeper correlation with cardiovascular risk, reproducibility and greater statistical power (O'Brien et al., 2013). Using ABP monitoring as the reference, clinic BP monitoring had a mean sensitivity of 74.62 (95% CI 60.72, 84.83) and specificity of 74.61 (47.88, 90.38) (Hodgkinson et al., 2011).

Diurnal variation (most notably during sleep), age, and race (Mancia et al., 1983) are significant individual factors impacting on BP readings. Typically BP naturally declines (10/5 mmHg or greater) in the transition from awake to sleep, referred to as “dipping” (O'Brien et al., 1988). A sub-group of the population does not experience dipping - ‘non-dippers’ - who have been noted to have a higher frequency of stroke, and thus are a clinically significant group to identify (O'Brien et al., 1988). Methods of BP monitoring should therefore give consideration to identifying diurnal variation in participants, and ABP fulfills this criteria.

As well as environmental conditions, equipment may impact on the accuracy of BP



measurement. The British Hypertension Society (BHS) have published an independent validation protocol for commercial BP monitors to ensure minimum standards of accuracy and precision (British Hypertension Society, 2013). For ongoing validity of measurements, all BP monitors also require regular calibration (British Hypertension Society, 2013). In addition, an appropriate cuff and bladder size should be used for the arm the BP device will be fitted to (O'Brien et al., 2013).

## **2.5.2 Blood pressure methods used in Chapter 3 (Cardioprotective dietary study)**

### **2.5.2.1 Clinic blood pressure measurements**

Seated and supine clinic BP measures were taken at the baseline visit and again at endpoint (12 weeks later). Blood pressure and heart rate were measured using an automated oscillometric upper arm BP monitor (OMRON 705CPII or equivalent, approved for use in the clinical setting by the British Hypertension Association). The monitors were calibrated within two years of previous calibration according to the manufacturer's instructions (Omron Healthcare, 2013). Seated measures were taken after 10 minutes of rest. The participant was seated comfortably with legs uncrossed and feet flat on the floor. The measurement was taken on the non-dominant arm using an appropriately sized cuff. Blood pressure was measured three times at two minute intervals; the value for the first reading was discarded and the mean for the two following readings was taken (O'Brien et al., 2003). Where the readings were more than 10% different, further measurements were taken until two consecutive readings met the criteria.

### **2.5.2.2 Ambulatory blood pressure measurements**

Ambulatory blood pressure (ABP) was measured using an automated ABP monitoring device (A&D TM-2430, BHS-approved). The device was calibrated yearly according to manufacturer's instructions (A & D Company, 2013). The monitor was programmed to take measurements every 30 minutes during the day between 0700 and 2200 hours, and every hour overnight (2200 – 0700). The first hour of readings were discarded (O'Brien et al., 2013).

Participants were educated in how to fit, start and stop the ABP monitors at their first baseline visit, alongside written instructions. Specifically they were instructed to stop what they were doing and relax their arm whilst a measurement took place. Ambulatory BP monitors fitted with an appropriately sized cuff (standard or large) and a diary card were sent to participants and subsequently self-fitted by participants on the morning of the measurements and worn for 25 hours until the following morning. Ambulatory BP measurements were made alongside the 24-hour urine collection (Appendix 2.1). Participants were asked to complete a diary card following each cuff inflation with the activity they were doing immediately prior to the measurement and to record when they went to bed and woke up.

Once returned, ABP data were downloaded and saved in de-identified form. The time the participant went to bed was logged into the software to manually identify sleep and awake BP measurements. A trained operator visually inspected the readings and removed those identified as artefacts (ie those readings where SBP was above 240 mmHg and below 50 mmHg, and DBP

readings that were above 140 mmHg and below 40 mmHg (Casadei et al., 1988).

### 2.5.3 Large arterial (vascular) function

Measures of arterial stiffness assess both structure and function of the artery, and there are a number of different methods available including pulse wave velocity (PWV), pulse wave analysis (PWA) and digital volume pulse (DVP). Table 2.4 summarises the indices measured with each of these methods.

Table 2.4 Methods for measurement and indices of vascular function

Index	Description
<b>Pulse wave velocity</b>	PWV is a measure of the arterial pulse transit time along the vessel segment analysed.
Carotid to femoral pulse wave velocity (PWVc-f)	A measure of central arterial (aortic) stiffness, and represents the time taken for the arterial pulse to propagate from the carotid to the femoral artery (Millasseau et al., 2005). An arterial tonometer (SphygmoCor) for recording pressure waveforms measures from the base of the carotid waveform to the base of the femoral waveform using sequential recordings referenced to an electrocardiogram. Transit time is assessed using an algorithm (Weber et al., 2009).
<b>Pulse wave analysis</b>	The high fidelity electronic recording of the contours of peripheral arterial waveforms from the radial, carotid or femoral arteries using applanation tonometry (Wilkinson et al., 1998).
Augmentation Index (AI)	AI is an indirect measure of arterial stiffness, calculated as augmentation pressure divided by pulse pressure and expressed as a percentage (Fantin et al., 2007). The AI represents pressure wave reflection within the systemic circulation (Munir et al., 2008).
Aortic AI	Pressure wave reflection as calculated from the carotid pulse; calculated as the ratio of the augmentation pressure to central pulse pressure.
Peripheral AI	Pressure wave reflection as calculated from the radial pulse; calculated as the ratio of the height of the late systolic pressure in the peripheral pulse to the peripheral pulse.
<b>Digital Volume Pulse (DVP)</b>	A measure of the smooth muscle tone of large arteries, DVP resembles the carotid pressure wave (Millasseau et al., 2005). It is obtained by photoplethysmography (passing an infrared light through the finger) which allows contour analysis of the pulse.
Stiffness Index (SI)	The SI is derived from analysis of the peaks of the DVP and relates to the stiffness of muscular-elastic (large) arteries. It is calculated by dividing the height by the peak-to-peak time, and expressed in metres/ second (m/s). The SI correlates with large artery PWV and is numerically similar to PWVc-f but not identical (Millasseau et al., 2006).
Resistance Index (RI)	The RI is defined as the ratio of the reflected wave to the first peak of the DVP (Millasseau et al., 2006) and is usually expressed as a percentage. RI is more strongly related to the vascular tone of small arteries and is particularly sensitive to drugs influencing vasomotor tone (vasoconstrictors and vasodilators) (Millasseau et al., 2002).

When pressure increases in the aorta during systole, the increase in pressure is not instantly

transmitted to the peripheral circulation but travels as a forward-going pressure wave at a speed known as the 'pulse wave velocity' (PWV; Table 2.4). Due to the direct relationship between velocity and elasticity (O'Rourke, 2006) it provides an accurate indication of arterial stiffness. It is considered a gold standard measure and is convenient because of its non-invasive nature, ease of determination, reliability and large body of evidence demonstrating its relationship with incident CVD across different population groups (The Reference Values for Arterial Stiffness Collaboration, 2010, Laurent et al., 2006).

Pulse wave analysis (PWA) measures vascular resistance from the augmentation index (AI) (Jennings et al., 2012) (Table 2.4). Left ventricular ejection generates a pressure wave that travels outward to the periphery of the circulation. This pressure wave is then reflected back from small arteries mainly in the lower body. The pressure waveform at any point in the vascular tree is thus a composite of a forward going wave and a reflected wave. Normally the reflected wave returns to the heart in diastole increasing myocardial perfusion. With increased vascular tone and arterial stiffening the reflected wave arrives earlier in systole reducing myocardial perfusion during diastole and imposing a higher load on the heart during systole (Chowienczyk, 2011).

The gold standard measurement of AI is calculated based on the direct measurement of the aortic pulsewave located near the heart, however this is impractical due to its invasive nature. Instead, pressure wave reflection can be quantified using applanation tonometry recordings of high fidelity waveform from an accessible pulse (Chowienczyk, 2011). Peripheral AI has recently been recognised as a useful adjunct to Aortic AI, due to its close relationship to Aortic AI as well as its reflection of central SBP (Chowienczyk, 2011). As they are calculated as ratios, AI measures are dimensionless and usually expressed as a percentage (Laurent et al., 2006).

Digital volume pulse (DVP) waveform is another non-invasive and simple measure of arterial function, sensitive to changes in arterial stiffness resulting from alterations in smooth muscle tone of large arteries (Millasseau et al., 2000) (Table 2.4).

## **2.5.4 Vascular function: methods used in cardioprotective dietary study**

### **2.5.4.1 Pulse wave velocity**

PWVc-f was assessed using a non-invasive SphygmoCor VW apparatus with Sphygmocor analysis software (SphygmoCor version 7.01 AtCor Medical Pty, Australia). PWVc-f is computed as the time delay between the upstroke of the arterial pressure wave at the carotid and femoral arteries and the anatomical carotid to femoral distance. The distance between the surface markings of the sternal notch and the femoral artery site was used to estimate the difference in path length between the arteries in order to calculate PWVc-f .

In line with agreed methodology (The Reference Values for Arterial Stiffness Collaboration, 2010), standardised conditions for measurement including consistent room temperature, period of rest prior to measurement, time of day, position, length of time abstaining from eating and alcohol, and avoidance of speaking and sleeping during the measurement (Laurent et al., 2006)

was enforced. On each occasion participants were rested in the supine position for 15 minutes and BP was recorded using an automated sphygmomanometer (Omron 70CP or equivalent auto upper arm BP monitor). Up to six measurements of PWVc-f were made with the criteria that the coefficient of variation was less than 5% for three measurements for the results to be acceptable.

#### **2.5.4.2 Pulse wave analysis**

Vascular visits were conducted at Week 0 (baseline) and Week 12 (endpoint) and participants were rested in the supine position for another 15 minutes and BP was recorded using an automated sphygmomanometer (Omron 70CP or equivalent). Resistance vessel tone was determined from the AI using the Sphygmocor VW apparatus (Kelly et al., 2001). Pressure wave reflection was quantified by measuring AI from the carotid to radial pulse waveform using the SphygmoCor<sup>TM</sup> VW apparatus with SphygmoCor analysis software (PWV Medical, PTY, Australia) in the PWA mode. Up to six measurements of AI were made with the criteria that the coefficient of variation was less than 5% for three measurements for the results to be acceptable. Central and peripheral mean arterial BPs were estimated from the supine BP and carotid-radial pulse wave measurements using the SphygmoCor software.

#### **2.5.4.3 Digital volume pulse**

A photoplethysmograph (PulseTrace, Micro Medical Ltd, Gillingham, Kent, UK) was placed on the index finger of the right hand to obtain the digital pulse volume (DVP) and was used to calculate stiffness index ( $DVP_{SI}$ , m/s) and reflection index ( $DVP_{RI}$ , %). Blood pressure and DVP waveforms were recorded over 10 second periods after 5, 10 and 15 minutes and the average peak-to-peak time (PPT) at 5, 10 and 15 minutes was calculated using the PulseTrace Software (Micro Medical).  $DVP_{SI}$  index was calculated by dividing the PPT value into height in metres and multiplying by 1000 into m/sec and  $DVP_{RI}$  is the height of the pulse notch expressed as percentage of the systolic pulse wave.

### **2.5.5 Endothelial function**

The vascular endothelium is involved in regulating vasomotor tone, thrombosis and platelet aggregation (Ross, 1999). Endothelial dysfunction is the breakdown of this regulatory function and the start of the atherosclerotic process (Yeboah et al., 2009). As such, impaired endothelial function plays a central role in atherogenesis and also increases risk of arterial thrombosis. Although it is established as a significant indicator of incident cardiovascular events, it is not used clinically as it does not increase the prognostic accuracy of traditional risk prediction models (Yeboah et al., 2009).

The capacity of the vascular endothelium to synthesise nitric oxide (NO) and NO bioavailability are important determinants of normal endothelial function. Nitric oxide, synthesised from arginine in endothelial cells, regulates vessel tone and has anti-atherogenic properties. Many blood vessels respond to an increase in flow (shear stress) by dilating (Corretti et al., 2002) through the action of nitric oxide. Impaired production of nitric oxide results in endothelial dysfunction and an increased risk of CVD (Yeboah et al., 2007).

Flow mediated dilation (FMD) of the brachial artery measures the capacity of the vascular endothelium to synthesise NO (Donald et al., 2008). FMD is a non-invasive technique to measure the change in diameter of peripheral conduit arteries following a period of distal limb ischemia (Thijssen et al., 2011). Although the brachial artery tends not to be affected by atherosclerosis, brachial artery FMD is strongly correlated with the endothelium-dependent responsiveness of the coronary arteries and is regarded as the most robust method to measure endothelial function (Hall, 2009). Impaired FMD has thus been proposed to be associated with the risk of atherosclerotic disease (Peters et al., 2012)

FMD has been used in a number of intervention studies (Sanders et al., 2011, Shechter et al., 2009, Yeboah et al., 2007, Yeboah et al., 2009, Rossi et al., 2008), however a lack of standardization of protocols and differing methodological approaches means that results between studies are inconsistent and the outcomes are not easily compared (Thijssen et al., 2011). Some methodological differences noted in the literature include physiological variability which can be controlled by standardizing temperature, recent food and drink intake, and avoiding measurements soon after exercise or during illness (Deanfield et al., 2007).

### **2.5.6 Endothelial function - measurements in the cardioprotective dietary study**

Participants abstained from alcohol and strenuous activity 24-hours prior to the clinic visits and were provided with a low-fat ready meal (10 g fat, 3 MJ) to consume in the evening (before 2100) and then fasted overnight consuming no fluid other than water until attending the facility between 0800 and 1000 the next day. After 30 minutes supine rest in a temperature-controlled room (23 °C), measurements were made of endothelium-dependent and -independent vasodilation of the brachial artery using the FMD technique.

Endothelial function was assessed at the baseline and endpoint vascular visits (week 0 and 12 respectively) by measuring FMD of the brachial artery according to current guidelines (Corretti et al., 2002). A BP cuff or tourniquet was placed on the lower arm, about 5 cm below the antecubital fossa. High resolution ultrasound (Siemens Accuson CV70) system with 7-10 MHz linear array transducer, positioned by a stereotactic manipulator, was used to scan the brachial artery in a longitudinal section 2 to 15 cm above the elbow for around two minutes, to allow the diameter of the artery in diastole to be measured from the image after the procedure was completed. After optimal positioning of the transducer a baseline scan was recorded. Increased flow was then induced by inflation of a pneumatic tourniquet placed around the forearm (distal to the arterial segment being scanned) to a pressure of 250 mmHg for five minutes, followed by release. Images of the artery were taken until around two minutes after the cuff was deflated.

These images were then analysed to determine the maximal diameter of the artery to allow FMD to be presented as the change in post-stimulus diameter as a percentage of the baseline diameter (% FMD):

$$\frac{\text{Maximum diameter} - \text{Baseline diameter}}{\text{Baseline diameter}} \times 100\%$$

(Yeboah et al., 2007).

A second scan was commenced 10 seconds before release of the cuff and continued for three minutes after cuff deflation. After 10 minutes, to allow vessel recovery, another resting scan was taken. Sublingual glycerol trinitrate (GTN, 25 µg) was then administered, and a final scan performed three to four minutes later. Images were coded and recorded on VHS videotape, then digitised for subsequent blinded analysis using automated edge detection software (Brachial Analyser, Medical Imaging Applications, LCC, Iowa, USA). FMD was expressed as the percentage increase in brachial artery diameter from baseline to maximal dilation which occurs 30 to 90 seconds after release of the cuff. Dilation to GTN was measured as an independent measure of vascular smooth muscle function (Ducharme et al., 1999), and was calculated in the same way as % FMD but expressed as % GTN (ie the percentage increase in brachial artery diameter from baseline to maximal dilation after GTN).

### **2.5.7 Blood lipids**

Hyperlipidaemia, specifically abnormalities in serum cholesterol, some lipoproteins and TGs, is a long-standing marker of cardiovascular risk (Ingelsson et al., 2007). The most commonly measured lipids for the assessment of cardiovascular risk are serum total cholesterol (the main carrier for circulating cholesterol from the liver); and HDL-cholesterol (responsible for 'reverse cholesterol transport' ie the removal of cholesterol from tissues for return to the liver). Laboratory methods for total and HDL cholesterol measurements enable LDL-cholesterol to be calculated (given the total cholesterol and TGs).

Factors of importance to determining risk include the relative proportions of LDL-cholesterol and HDL-cholesterol; the size of circulating lipoproteins, in particular elevated small dense LDL particles which are known to be associated with increased risk; and TG rich lipoproteins which are reflected by plasma concentrations of non-HDL cholesterol and apo B (Watts and Karpe, 2011). Similarly apo A1 is the major structural protein component of HDL particles and as such is thought to be an important marker of risk (van der Steeg et al., 2007). The ratio of apo B to apo A1 (Apo B:A1) is sometimes considered a better marker of risk than more traditional cholesterol measures in some studies, and in particular is useful in guiding clinicians in the monitoring of effectiveness of statin treatment (Sniderman et al., 2003) although its superiority in the clinical setting is not conclusive (Ingelsson et al., 2007).

High serum TGs have long been associated with elevated cardiovascular risk, although the efficacy of serum TGs in predicting risk have been the subject of some controversy in the literature due to the intra-individual variability which make them a weaker epidemiological risk factor compared to a more stable factor such as HDL cholesterol (Watts and Karpe, 2011). Despite the controversy, higher TGs are now widely accepted as important for the evaluation and management of cardiovascular risk (Miller et al., 2011). TG transport in blood is through two main particles, chylomicrons and very low density lipoproteins.

## **2.5.8 Blood lipid measurements used in cardioprotective dietary study**

### **2.5.8.1 Collection of blood samples**

Blood samples for analysis of cholesterol, apo-lipoproteins and TGs were drawn from participants, after an overnight fast, at the vascular visits (baseline and endpoint) by a trained phlebotomist. The vacutainer method (Beckton-Dickinson) was used for collecting blood samples into gold top tubes which contains a serum separating agent.

### **2.5.8.2 Processing of blood samples**

Whole blood samples were sent to the laboratory without any processing.

Samples for serum collection were allowed to stand for approximately 30 minutes at room temperature before being spun in a centrifuge at 3000 rpm for 20 minutes, at 4°C. After centrifuging, serum was then separated into pre-labelled aliquot tubes and stored at -70°C. Serum samples were sent in batches, over four cohorts (Cohort 1: August – December 2010; Cohort 2: January – June 2011; Cohort 3: July – December 2011; Cohort 4: January to June 2012) to the Clinical Chemistry Department at King's College Hospital for analysis.

### **2.5.8.3 Analysis of blood samples**

Triglycerides, total and HDL cholesterol were measured in serum by enzymatic methods on an automated chemistry analyser. Spare samples were kept frozen in case of analysis problems. The measurements were conducted in a Clinical Pathology Accredited laboratory at King's Health Partners. Precision estimates were based on each sample assayed two times per run, two runs per day, for at least ten days and computed according to Clinical and Laboratory Standards Institute specifications (Document EP05.A2, Evaluation of Precision Performance of Quantitative Measurement Methods: Approved Guideline).

The ratio of total cholesterol to HDL cholesterol was selected as the lipid primary outcome, as it represents the best lipid metric of risk (Lewington et al., 2007). Cholesterol analysis was undertaken on serum using enzymatic procedures (Allain et al., 1974) on an automated chemistry analyser.

For measurement of total cholesterol an enzymatic, colorimetric reaction was used (Siemens Medical Solutions Diagnostics Europe Ltd). The intra-assay coefficients of variation (CVs) for total cholesterol as supplied by the manufacturer was 0.6% at each of three different levels: 3.9, 5.2 and 5.7 mmol/L; and the inter-assay CVs were 1.1%, 1.5%, 1.0% respectively (Siemens, personal communication, 2014).

Measurement of serum HDL cholesterol was undertaken using a two step enzymatic, colorimetric automated procedure (Izawa et al., 1997) (Siemens Medical Solutions Diagnostics Europe Ltd). The intra-assay coefficients of variation (CVs) for HDL cholesterol as supplied by the manufacturer was 1.1%, 1.4% and 1.5% respectively at each of three different levels: 0.91, 1.39 and 1.95 mmol/L; and the inter-assay CVs were 2.2%, 2.1%, 2.5% respectively (Siemens, personal communication, 2014).

LDL cholesterol was determined directly using an enzymatic, colorimetric method, without the need for sample pre-treatment (Okada et al., 1998) (Siemens Medical Solutions Diagnostics Europe Ltd). The intra-assay and inter-assay (over 10 different days) CV for a low mean LDL concentration (1.22 mmol/L) are 1.52% and 1.61% respectively; for medium mean LDL concentration (2.95 mmol/L) the CV are 0.66% and 1.76% respectively; and for high mean LDL concentration values a CV of 0.70 and 0.45% for intra-assay and inter-assay respectively (Okada et al., 1998).

Apo A1 and Apo B were measured on the Siemens Advia 2400 using reagent supplied by Siemens Medical Solutions Diagnostics Europe Ltd. Apo A1 and Apo B were analysed on the ADIVA 2400 using a polyethylene glycol (PEG) enhanced immunoturbidimetric assay with reagents supplied by Siemens Medical Solutions Diagnostics Europe Ltd.

An enzymatic, colorimetric method was used for the measurement of TG (McGowan et al., 1983). Within-run and between-run precision of the method at low concentrations (570-600 mg/L) gave coefficient of variations (CV) of 2.6-3.3%; at medium concentrations (1,120 – 1,090 mg/L) a CV of 2.0-2.3%, and at high concentrations (10,930 – 11,630 mg/L) a CV of 1.3-2.3% . TG reagent was supplied by Siemens Medical Solutions Diagnostics Europe Ltd.

## **2.6 Anthropometry measures used in the cardioprotective dietary intervention**

### **2.6.1 Height**

Height was taken by a trained researcher in the morning, using a fixed stadiometer that had been calibrated. To ensure the volunteer stood upright, heels and shoulders were firm against the measuring rod, knees and back were straight and the participant was asked to look forward with the head in the Frankfurt Plane position. The measuring slide was then pushed slowly onto the head so that it was touching without bending and the height from the mark displayed was recorded to one decimal place.

### **2.6.2 Weight**

Weight was taken in kilograms on portable digital weight scales (Tanita, Netherlands), which were regularly calibrated according to manufacturer recommendations. A tare of 1kg was applied each time to account for clothing that could not be easily removed. Weight measurements were taken first thing, in the morning, after an overnight fast and with an empty bladder. The scales were placed on a firm, level surface and the participant removed shoes and any outer clothing, then stepped on to the platform and remained still, until the readout on the scales became stable. The weight was then read from the display and recorded to one decimal place.

### **2.6.3 Waist circumference**

Waist circumference was taken at the mid-point between the lower rib margin and the iliac crest in centimetres, using a tape measure and pen to mark the point of measurement (Molarius et al., 1999) as recommended by the WHO Expert Consultation Group (World Health Organization,



2011). The waist circumference was measured on participants with their waist uncovered to the nearest 0.1 cm, or where not possible to measure the waist uncovered, then the measurement was made on the participant after heavy outer garments had been removed and with all tight clothing, including the belt, loosened and the pockets emptied. Participants stood with their legs shoulders-width apart and their weight equally distributed on each leg with the arms to the sides. Participants were asked to breathe normally and the reading was taken at the end of a normal exhalation. The tape measure was held closely against the body and placed horizontally at the desired height, the measurement was then read from the tape measure and recorded to one decimal place.

## **2.7 Qualitative research methods**

Qualitative research is concerned with the systematic collection, analysis and interpretation of data that is not numerical. It involves concepts and behaviours of people in a social world (Lim et al., 2012). The use of qualitative research has grown in healthcare, and is particularly useful in the field of nutrition and dietetics which is concerned with behavior change (Pilnick and Swift, 2011). There is a growing recognition of the need to use both qualitative and quantitative methods in an integrated way. The addition of qualitative methods can highlight the human dimension of interventions, providing important contextual data for the translation of interventions that are often tested under unrealistic standardised conditions in quantitative studies (Burke Johnson and Onwuegbuzie, 2004, Tripp-Reimer and Doebbeling, 2004).

Ensuring the rigour of qualitative research requires a different approach to that of quantitative methods which are concerned with constructs of validity, reliability and generalizability. As qualitative research assumes a relativist ontological position (belief in a socially constructed reality), guidelines reflect different quality criteria (Pilnick and Swift, 2011). In response to concerns about the academic rigour of some published reports, there have been a number of attempts to clarify quality criteria for qualitative research (Table 2.5).

Within qualitative research, the research team is acknowledged as having a close engagement with the whole research process and personal bias is therefore unavoidable. To deal with this issue, it is imperative that the identity, qualifications, gender, experience and training is clarified for the reader (Tong et al., 2007). This is a concept known as 'positionality'. In terms of study design, the research position and methodological paradigm should be clearly stated (Tong et al., 2007), along with the theoretical framework underpinning the research.

Interviews are one of the collection methods used in qualitative nutrition research, and may be conducted face-to-face, by telephone or online. They range from unstructured in-depth interviews, predominantly led by the person being interviewed, to fully structured interviews consisting of pre-defined questions administered using exactly the same phrasing and in the same order by the researcher, with the interviewee having little control over topics covered. Semi-structured interviews fall between these two ends of the continuum, with a clear list of topics and questions developed in advance of the interview but with some flexibility in how the questions are phrased and their order. The interviewer is also free to probe the interviewee further on their responses (Draper and Swift, 2011).

Interviews should be recorded, and transcribed into words and phrases. Thematic analysis, a systematic approach to identify and describe patterns in the data, is often used in qualitative research (Braun and Clarke, 2006). The researcher takes a central role in analysis, which may be 'literal' (whereby the researcher will bracket out their own interpretation of the data during analysis) or 'interpretative' using reflexivity. Reflexivity refers to the transparent process of reflection and is an acknowledgement of the researcher's role in the data analysis process. It is a means by which the researcher can accurately report their role in the research process, and is an essential component of qualitative research methods (Fade and Swift, 2011).

### 2.7.1 Positionality, research paradigm and methodological position used in Chapter 4

The primary researcher was the CRESSIDA study (Chapter 3) dietitian, responsible for developing the cardioprotective dietary intervention, strategies for implementing the intervention, and delivery of the intervention throughout the 12 weeks of the study. For this qualitative study, she also developed the research protocol and interview schedule, interviewed the participants, checked the transcripts and led the development of themes from the data. Investigator triangulation was achieved through reaching agreement with an undergraduate student researcher who undertook transcription and independently analysed the data units (Reeves et al., 2008).

Table 2.5 Criteria for assessing qualitative research

<b>Qualitative research review guidelines (RATS) (Clark, 2003)</b>	
1. <b>Research question:</b>	interesting, relevant, explicit, justified & linked to existing knowledge.
2. <b>Appropriateness of qualitative methods:</b>	description and justification of use of qualitative methodology, appropriate for study aim.
3. <b>Transparency of:</b>	
	<i>Sampling:</i> appropriate for knowledge sought, study sample criteria justified and explained.
	<i>Recruitment:</i> methods, selection & sampling, details of recruitment - how and by whom.
	<i>Data collection:</i> systematic & comprehensive; study group & setting characteristics clearly described, why & when data collection stopped, methods outlined including examples (eg interview questions), end of data collection justified and described.
	<i>Role of researchers:</i> appropriate researcher/s, potential bias, data collection, and interpretation.
	<i>Ethics:</i> informed consent, confidentiality, ethics committee approval.
4. <b>Soundness of interpretive analysis:</b>	
	<i>Analysis:</i> (eg thematic) appropriate for study, interpretation presented & supported, appropriate & effective use of quotes, reliability of data & interpretations checked eg independent analysis & review of themes.
	<i>Discussion &amp; presentation:</i> Findings presented with reference to existing literature and contribution, strengths & limitations explicitly discussed, manuscript well written & presented, red flags checked eg jargon, over-interpretation or superficial analysis.
<b>Consolidated criteria for reporting qualitative research (COREQ): 32-item checklist for interviews and focus groups (Tong et al., 2007)</b>	
1. <b>Research team and reflexivity</b>	
	<i>Personal Characteristics:</i> description of interviewer, including gender, educational credentials, occupation, previous training and experience.
	<i>Relationship with participants:</i> description of interviewer's relationship with participants prior to study; participant knowledge of interviewer including personal goals, reasons for research; assumptions & interests of researcher
2. <b>Study design</b>	
	<i>Theoretical framework:</i> methodological orientation and underpinning theory stated.
	<i>Participant selection:</i> Methods of sampling, approaching participants, sample size, number

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who declined or withdrew.

*Setting:* Where data was collected, who else was present, sample characteristics eg demographic data

*Data collection:* Interview guide, audio or video recorded, if field notes were made and when, length of the interviews, data saturation discussed, if transcripts were returned to participants for comment or correction.

### 3. Analysis and findings

*Data analysis:* number of data coders, description of coding, if themes identified in advance or derived from data, if software was used to manage data, participant feedback on findings.

*Reporting:* quotations used to illustrate the themes, identified by participant number;; clarity of major themes & description of diverse cases or discussion of minor themes.

### **Qualitative research in nutrition and dietetics: assessing quality (Pilnick and Swift, 2011)**

1. **Clarity of methods** of data collection and analysis: presents sufficient information on how the data were collected and analysed; why collected and analysed in the chosen way.
  2. **Reflexivity:** recognition of (a) impact of the researcher, as well as the professional, intellectual and personal baggage the researcher brings to the analysis (eg age, gender, social class) as well as the 'distance' (social, cultural) between the researcher and the participants; (b) participants' active involvement and purposeful engagement in producing the activities studied (ie why people behave as they do in the context of a study is in itself a key analytical question).
  3. **Dealing with negative cases:** research findings based on critical investigation of the whole data, not just a selective set of examples; consideration of negative cases that don't fit and potential reasons for discrepancies.
  4. **Fair dealing:** all responses are dealt with equally; responses from one group of participants not favoured over others.
  5. **Worth or value:** outline of what the research adds to the existing evidence base is included.
- 

Research paradigms can be characterised through their ontology, epistemology and methodology (Guba, 1992). A mixed-paradigm research model was adopted combining the interpretivist and positivist approaches (Schensul, 2012) which drove the methodology selection. Set in the context of the background and experience of the dietitian researcher, an interpretivist method, ie 1:1 interviews, was naturally adopted as the most useful path to understanding the experience of participants who had recently undergone dietary change. However, given the topic being explored, the experience of the researcher in facilitating dietary change and her science background in nutrition and dietetics, a positivist paradigm underpinned the methodology, and a semi-structured interview (rather than the option of an open interview without structure) was considered appropriate.

The researcher did not approach the data with a series of hypotheses to be tested but instead used the data to generate an explanation (Fade and Swift, 2011) about factors that might have been important in enabling the dietary change and factors that may have been barriers. However, given her experience and relationship with the participants, she came to the data with preconceptions about some of the factors that may have aided dietary change for the participants, as well as some of the challenges they experienced, and this guided the interview topic list. Analysis was guided by interpretive phenomenology, as the research aimed to capture the experiences of the participants as they underwent dietary change (Braun and Clarke, 2006).

### **2.7.2 Qualitative data analysis**

A thematic style of analysis was adopted, as the aim of the research was to explore participants' experiences of the dietary intervention and thematic analysis is a method for identifying, analysing and reporting patterns by the researcher (Fade and Swift, 2011). There were no pre-

determined themes to explore, however the research topic encompassed an interest in discovering aspects of the diet that were easier or harder to adopt; identifying enablers and barriers to making the dietary changes and understanding the participants' perceptions about the advantages and disadvantages of making the dietary changes. Analysis was guided by an interpretivist paradigm, which accepts the subjectivity of the analysis and does not attempt to remove researcher preconceptions or influence from the analysis (Fade and Swift, 2011).

A systematic approach to thematic analysis was taken using the constant comparative analysis method (Glaser, 1965). Each data item (interview transcript) was read multiple times, and at least once whilst also listening again to the audio recording, in order to develop familiarity with the data (Fade and Swift, 2011). Line-by-line inductive coding was undertaken manually by the dietitian researcher and the student dietitian researcher independently. Frequent discussions on codes, and later themes, between the dietitian and student dietitian researcher were used to reach agreement on the analysis with the aim of achieving investigator triangulation (Reeves et al., 2008).

Extracts that were single words, groups of words or sentences which were identified as potentially meaningful or interesting were initially highlighted and notes made in the margins of the transcripts (Fade and Swift, 2011). Using an Excel spread sheet, initial codes were generated from each interview; these were then collapsed into potential themes as the codes were synthesised and analysed to determine meaning. A list of candidate themes, sub-themes and related codes were produced, which were later refined through an iterative process collapsing and separating them after further interpretation (Braun and Clarke, 2006) to achieve a higher level, smaller set of concepts (Glaser, 1965). Themes were then named and a conceptual diagram generated to represent relationships between them. A brief analysis of gender differences across the themes was also undertaken, as during the data analysis process it became apparent that some themes appeared more strongly in transcripts with participants of one gender over the other.

### **2.7.3 Presentation of qualitative findings (Chapter 4)**

Data was analysed and the findings of the research reported in an integrated *Findings and Discussion* section in Chapter 4 to assist with the synthesis of results for the reader. This makes a separate discussion section unnecessary (Burnard, 2004).

## **2.8 Dietary costing methods**

Food cost studies vary in the approach to data collection, either attempting to estimate actual costs of foods as consumed by individuals, or alternatively the theoretical costs of a given dietary pattern or basket of foods. Studies which have used actual costs of diets typically use shopping receipts or expenditure diaries from participants (for example, in the UK Family Food Survey (Office for National Statistics, 2013a)). Alternatively an approximation of food spending can be made by applying food price databases to food intake diaries (Andrieu et al., 2006, Schröder et al., 2006), food frequency questionnaires (Cade et al., 1999, Lopez et al., 2009, Goulet et al., 2008, Aggarwal et al., 2011) and 24-hour recall data (Waterlander et al., 2010, Rydén et al.,

2008). As well as different methodological approaches, food price databases used across different studies vary in the year and unit of currency, making comparability of results difficult (Rao et al., 2013) and variability in the food economy across different countries further confounds pooling of results (Office for National Statistics, 2013c).

The unit measure of cost used is another common source of variation between studies, impacting on the findings depending on the metric used. Cost per unit of energy is a relatively common measure of cost used (Monsivais and Drewnowski, 2009, Drewnowski, 2010), which may or may not be adjusted for total energy intake in an effort to remove the potential for greater dietary costs for those consuming greater numbers of calories. Alternative units of dietary cost are price per edible weight of foods purchased (cost of a food item as consumed) or price per portion (cost per average serving amount consumed) (Carlson and Frazão, 2012).

Although popular, there are a number of problems with using price per calorie as a metric for studying the cost differential between healthy and less healthy dietary patterns including the mathematical properties of the measure, and the impracticality in terms of consumer purchasing costs and behaviour. Firstly, the mathematics of the unit is that calories appear both in the numerator of the energy density calculation as well as in the denominator of the metric used, which results in an inverse proportion between kcal/g and price/ kcal (Lipsky, 2009). Thus price per unit of energy will always increase as energy density decreases because of the algebraic properties of the ratios used. Carlson and Frazão demonstrate this nicely by comparing the price per calorie of whole and skim milk, which clearly favours a lower price for whole milk however if the same given quantity of whole and skim milk is purchased, the price to the consumer is invariably the same (Carlson and Frazão, 2012). Secondly, the price per calorie does not take account of the practical amounts eaten of a particular food, and therefore misrepresents the likely cost to consumers. For example a portion of crisps providing 100kcal would be around 19g, less than the weight of single bags in the UK, whereas 335g of strawberries (around a punnet) would provide the same number of calories. Finally, it has been proposed that the use of low-calorie marketing claims by manufacturers means that is unlikely that price per calorie is a major determinant of food choice of consumers (Lipsky, 2009). Food purchasing behaviour is known to be complex and multifactorial, accounting for personal preference, including taste and convenience, as well as health perceptions, availability, influence of other household members and availability of cooking and storage equipment (Lipsky, 2009). There is no evidence that consumers choose foods simply by calculating the cost per calorie as many studies might suggest (Frazão, 2009).

Some researchers argue that dietary costs should be adjusted for energy intake to allow comparability across different energy intakes, in line with convention when comparing nutrients across groups (Drewnowski et al., 2009). Others contend that consuming a greater number of calories will result in higher costs to an individual and therefore energy adjustment is inappropriate and misleading in the debate (Frazão, 2009). Furthermore many health-promoting foods, such as unprocessed fruit and vegetables, are lower in energy density; as energy density increases, total energy intake also tends to increase (Rolls, 2000). Many studies published in the literature have nevertheless presented dietary cost data adjusted for energy intakes (Andrieu et

al., 2006, Schröder et al., 2006, Drewnowski and Eichelsdoerfer, 2009, Waterlander et al., 2010, Lopez et al., 2009, Rydén et al., 2008).

Alternatives to the price per calorie metric are costing an average portion of a given food, or determining the price of the edible portion of foods by weight. The price of an average sized portion of a food may be most useful for consumers in comparing the price of different goods at the point of sale, as it does not rely on the consumer having an understanding of the weight of an average sized portion of a food compared to another food, and then being able to calculate the proportion of the cost that would be attributed to a single serving. This metric may also be useful when deciding if healthier foods are more expensive than less healthy options, although it is confounded by its lack of differentiation between a food that is low cost and a food that is eaten in small portions (Carlson and Frazão, 2012). Finally, price of edible weight has been proposed as a useful measure of costing foods when reporting dietary cost as it acknowledges that food preparation generally results in some loss of the original weight of the food purchased in the final product to be consumed. Using the edible weight price ensures consistency with methodological approaches to nutrient analysis of foods eaten, as it refers to the cost of the proportion of the purchased weight that is actually consumed rather than the cost of the weight purchased. For example, in the UK food tables, for raw food the edible portion refers to "...edible material remaining after inedible waste has been trimmed away"(McCance and Widdowson (eds), 2002). There are many foods where the edible portion differs from the purchased portion, for example canned vegetables, where the liquid is generally drained off and not consumed, leaving 0.64 of the purchased weight for consumption; a rasher of streaky bacon with the rind removed leaves only 0.86 of the amount purchased; and a baked kipper as eaten (without bones) represents 0.54 of the original weight purchased (Food Standards Agency, 2002). In addition, many foods lose weight in the cooking process, which must be accounted for when calculating food costs and nutrient composition (School Food Trust, 2008). This is the method chosen for the dietary costing study, as outlined in the following section.

## **2.8.1 Methods used in study to determine the cost of a cardioprotective diet (Chapter 5)**

### **2.8.1.1 Extraction of food codes and weights**

Food codes and portion weights were extracted into a spreadsheet for each participant from the 4-day food diaries completed by participants included in the sample, and previously entered into nutrient analysis software (NetWisp version 3.0; Tinuviel Software, UK). Each participant's food code list was then separated into baseline and endpoint sheets for detailed costing. A lookup function was used to cross reference between the food codes recorded by participants on each day of the baseline and endpoint diaries, and a purpose built food cost database (see 2.6.2.2 below).

Finally, each food code was assigned to one of twelve food groups (Table 2.6) according to the categorisation used in McCance and Widdowson food composition tables (Food Standards Agency, 2002).

Table 2.6 McCance & Widdowson (2002) food group categories assigned for analysis purposes

Cereals and grains	Fruit	Fats and oils
Dairy	Nuts	Non-alcoholic drinks
Eggs	Fish	Alcoholic drinks
Vegetables	Meat	Sugar and snack foods

### 2.8.1.2 Development of a food cost database

A food cost database was constructed by compiling a full list of food codes from the sample, de-duplicating repeat codes and de-coupling codes that incorporated more than one ingredient (for example potatoes mashed with butter was separated into the code for potatoes and a code for butter, and a formula to include 50g butter per kg of potatoes purchased was applied to the original code for costing purposes). Where ingredients as purchased required home processing, the edible portion of the whole food was used as a multiplication factor on the food weight.

Prices of the foods were then obtained from two online supermarkets (one identified as 'budget' and the other a mid-priced 'regular' supermarket) for all foods recorded by all participants (n=40) between January and March 2013. Prices were also obtained from two additional online supermarkets for all foods recorded by a smaller number of participants (n=12; distributed equally across both groups) to obtain a multiplication factor for another 'regular' supermarket as well as a higher priced 'quality' supermarket. Foods were priced using own brand products where available, or the brand available at the majority of the four supermarkets.

The cost of the food was based on medium sized packages, and where possible comparable package sizes were priced across supermarkets. Sale or multi-buy prices were disregarded and the usual selling price of the food item was used for the database. For food items that were provided to participants as part of the dietary intervention allocated, prices were obtained for the actual brand and package size provided and costed at the weight reported in the food records. The cost of food items purchased outside of the supermarket, for example fast food items, were obtained by comparing the cost of similar food items across four similar food outlets (such as fast food outlets). The cost per gram of the food was obtained by dividing the purchase price by the edible portion weight of the food.

### 2.8.1.3 Application of food prices to food intakes recorded in 4 day dietary diaries

For each participant at each time point, food costs were calculated by multiplying the weight of each food item consumed by the unit cost in pounds sterling from the matched code in the food database, and totalling the costs of all food and beverages consumed over the food days completed in each diary. For each participant diary, the mean of the supermarkets was calculated to obtain a mean total cost over four days, which was then converted to a mean daily cost.

The cost of home cooked dishes was obtained by using the recipe provided by the participant; if no recipe was provided a standard recipe was sourced from either the UK food tables (Food Standards Agency, 2002), a UK food industry recipe book (Campbell et al., 2008), or the BBC Good Food website (BBC Good Food). As for individual food items, the cost of recipes was based on edible portion of the food ingredient components.



## Chapter 3 Cardioprotective dietary intervention

### 3.1 Introduction

Much of the evidence informing public health messages about diet and CVD prevention is based on epidemiological observations with disease endpoints. Hypotheses generated from population level studies have been further investigated through a multitude of intervention studies that have been conducted with surrogate markers of risk, rather than clinical endpoints. Most intervention studies have focused on the impact of specific individual components of diet and the relationship to cardiovascular risk. These include studies manipulating the amount and type of dietary fat (Hooper et al., 2012), investigations into the effect of consuming regular portions of fish as well as supplemental fish oils (Hooper et al., 2004), the impact of whole grains on cardiovascular risk (Ye et al., 2012), and the BP response to restrictions of dietary sodium (He et al., 2013).

The use of surrogate endpoints, and the isolated nutrient approach of many of the intervention studies investigating dietary influences on cardiovascular risk, has led to apparent contradictions in the evidence. For example, a restriction on dietary salt intake is recommended in the dietary guidelines across a number of countries including the UK (Department of Health, 1994), United States of America (Dietary Guidelines Advisory Committee, 2010) and Australia (National Health and Medical Research Council and Department of Health and Ageing, 2013), however the effects of modest salt reduction on CVD outcomes are contentious when studies are pooled (Taylor et al., 2011). It has even been suggested that it may bring about detrimental effects on serum cholesterol and TGs (Graudal et al., 2012). Such contradictions are frequently exploited in the media jeopardising public confidence in national dietary guidelines (Neal et al., 2013).

In comparison to the breadth of intervention research investigating individual dietary components and CVD, relatively few well-designed studies have evaluated the role of overall dietary patterns (Williams et al., 2013). The landmark primary prevention study focusing on dietary patterns and cardiovascular risk was the DASH study, an intervention trial undertaken in the USA which encouraged increased intakes of vegetables, fruits, and low-fat dairy products, and the inclusion of whole grains, poultry, fish and nuts with reduced red meat, sweets and sugar sweetened beverages. It showed promising results for BP reduction in people with untreated pre-hypertension or stage 1 hypertension (Appel et al., 2006, Sacks et al., 2001). There have been a number of follow on studies to the original DASH trial, including one that has investigated the effect of the diet with different levels of sodium intake (DASH-Sodium trial) (Sacks et al., 2001), and another on different macronutrient proportions using DASH dietary principles (the OmniHeart study) (Appel et al., 2005). The DASH-Sodium study demonstrated additional BP lowering effects of the DASH diet when combined with lower intakes of sodium. The OmniHeart study compared the DASH dietary pattern at different macronutrient levels: one higher in protein (25% of energy from protein, compared to 15% in the other diets), a diet higher in carbohydrate (58% of energy, compared to 48% in the other two diets); and a diet higher in total and unsaturated fat (37% of energy from fat compared with 27% of energy in the other diets). Using a crossover design, all three diets were found to be favourable, but the modified macronutrient dietary patterns showed

slightly greater improvements in cardiovascular risk factors (Appel et al., 2005).

Both the DASH and OmniHeart Studies were relatively short-term, controlled feeding studies (ie all food and drink provided to participants for the whole of the study period). They demonstrated the potential value of adopting a dietary pattern approach with individuals at a pre-hypertensive stage. The PREMIER study demonstrated the effectiveness of a DASH dietary pattern in a free-living pre-hypertensive population with no controlled feeding and for a longer duration (6 month intervention) (Appel et al., 2003) but with less efficacy as the BP lowering effect of the diet was not as great as the previous trials.

Current population-level dietary advice reflects early recommendations issued by the Committee on Medical Aspects of Food Policy (COMA), and more recent guidance from the Scientific Advisory Committee on Nutrition (SACN). This advice is informed by the intervention studies discussed above, a mixture of research focused on individual dietary components as well as the dietary pattern research that has occurred in other countries. Specific dietary guideline recommendations are a reduction in total fat and *trans* fatty acids, the replacement of dietary SFAs with PUFAs or MUFAs, an increase in the intake of oily fish (dietary source of *n*-3 LCP), a reduction in dietary salt, and increased intakes of fruit and vegetables (Department of Health, 1994). In addition, the Department of Health also advocates a limit on NMES (Department of Health Committee on Medical Aspects of Food Policy, 1991) and an increase in whole grain consumption (Food Standards Agency, 2007). Despite the DASH diet being aligned with dietary guidance in the United Kingdom (UK), there has not been a well-conducted randomised controlled intervention trial in a free-living UK population to assess a dietary pattern that reflects this guidance.

### **3.2 Hypothesis**

An integrated dietary approach modifying the overall dietary pattern to conform with UK dietary guidelines for the prevention of CVD (5 portions of fruit and vegetables per day, increased consumption of whole grain cereals and oily fish; moderate total fat and reduced saturated fat, added sugars and salt intake) for a minimum of 12 weeks will lead to significant reductions in daytime systolic BP, a reduction in the ratio of total to HDL cholesterol (TC:HDL-C), and improvements in endothelial function compared to a representative UK diet in healthy adults aged 40 to 70 years.

### **3.3 Project aim**

The aim of the project was to undertake a randomised controlled trial comparing a cardioprotective dietary pattern with a control diet (a balanced diet representative of UK adults) in healthy, non-smoking adults aged 40-70 years at average risk of CVD. Primary outcomes included a change in daytime systolic BP, TC:HDL-C and endothelial function. Arterial stiffness indices were also included as secondary outcomes.

## 3.4 Methods

### 3.4.1 Study design

The study was a parallel 12-week randomised controlled dietary intervention trial. It was commissioned in response to the Food Standards Agency research requirement N02R0009 to “Study the effects of implementing current United Kingdom dietary recommendations on cardiovascular disease risk factors and vascular function”.

### 3.4.2 CRESSIDA study investigators

The study, known as the Cardiovascular disease risk REduction Study: Supported by an Integrated Dietary Approach (CRESSIDA), incorporated a team of researchers to undertake the research (Table 3.1). The author was responsible for the development and delivery of the dietary intervention, including all dietary visits throughout the study, collection and analysis of dietary data and the provision of food items to participants. In addition, she undertook study team tasks for study recruitment, screening, pre-baseline and baseline data collection, and assisted with other study tasks daily.

Table 3.1 CRESSIDA study investigators and research roles

Organisation	Role	Person
King's College London, Diabetes & Nutritional Sciences Division	Principal Investigator	Professor TAB Sanders
	Co-investigator & Study Coordinator	Dr Wendy Hall
	Co-investigators	Dr Sarah Berry Dr Louise Goff
	Postdoctoral Researchers	Dr Julia Darzi Dr Zoe Maniou
	Study Dietitian	Ms Dianne Reidlinger
	Technical Analyst & Vascular Technician	Ms Virginia Govoni
	Study Administrator	Ms Laura O'Sullivan
St Thomas' Hospital NHS Foundation Trust, Clinical Pharmacology, Cardiovascular Division	Laboratory Technician	Mr Robert Gray
	Co-investigator	Prof Philip J Chowienzyk
	Physiological Measurement Quality Control Officer	Ms Karen McNeill
St Thomas' Hospital NHS Foundation Trust, Division of Women's Health	Study Ultrasonographer	Dr Benyu Jiang Ms Louise Watt
	Study Statistician	Mr Paul T Seed
King's College Hospital, Clinical Chemistry Department	Study Clinical Biochemist	Ms Tracy Dew

### 3.4.3 Ethics and trial registration

Ethical approval was obtained from St Thomas' Hospital NHS Research Ethics Committee (Ref: 10/H0802/24). NHS Research and Development approval was also granted from the Guy's and St Thomas' Hospital NHS Foundation Trust. The study was formally registered as a randomised controlled trial (ISRCTN 92382106): <http://www.controlled-trials.com/ISRCTN92382106>.

### 3.4.4 Participants

Male and female participants were included if they were healthy, non-smokers and aged between 40-70 years. Participants between the ages of 40-70 years were chosen because risk increases markedly with age; an upper age limit of 70 years was selected because absolute annual risk of CVD exceeds 2% beyond that age in the majority of people and a higher proportion are receiving medication on daily basis. Potential participants were deemed ineligible if any of the specified exclusion criteria applied (Table 3.2).

Table 3.2 Exclusion criteria

- 
- A self-reported history of angina pectoris, myocardial infarction, stroke, peripheral vascular disease or congenital heart disease
  - Asymptomatic atrial fibrillation
  - Type 1 or Type 2 diabetes mellitus (fasting blood glucose > 7.0 mmol/L)
  - Seated Blood pressure >160/105 mmHg
  - Current use of medication for lowering blood cholesterol or blood pressure
  - BMI <18.5 and >35 kg/m<sup>2</sup>
  - An overall risk of CVD over the next ten years of >20%.
  - Clinical history of cancer (excluding basal cell carcinoma) in the past five years
  - Chronic renal, liver or inflammatory bowel disease
  - Current cigarette smoker (confirmed by urinary cotinine analysis)
  - History of substance abuse or alcoholism (previous weekly alcohol intake >60 units/men or 50 units/women)
  - Current self-reported weekly alcohol intake exceeding 21 units for women and 28 units for men
  - Currently pregnant, planning pregnancy or having had a baby in the last 12 months
  - Unwilling to follow the protocol and/or give informed consent
  - Unwilling to refrain from use of dietary supplements
  - Unwilling to restrict consumption of oily fish
  - Weight change of >3 kg in preceding 2 months
-

### **3.4.5 Sample size**

Sample size was estimated for a change in daytime SBP based on a treatment effect of diet on SBP of 4mmHg. Previous data with repeated measures of ABP monitoring under different dietary conditions for a similar population found mean values between 136.7 and 139.8 mmHg, standard deviation between 12.5 and 14.2 mmHg, with correlations between follow-up values of between 0.60 and 0.76, and between baseline and follow-up of between 0.66 and 0.72 (Berry et al., 2010). Taking median observed values in each case, and assuming analysis using analysis of covariance (ANCOVA), with at least one useful measurement at baseline and three at follow-up, it was assessed that full data on 78 people in each group (a total of 156 subjects) would be sufficient to detect the treatment effect at the 5% significance level with 90% power (Frison and Pocock, 1992). Additional power was gained by including the baseline variables used in the minimisation process (Senn, 2006).

### **3.4.6 Recruitment and screening**

Potential participants were recruited through two newspaper and one magazine advertisement, recruitment databases from previous studies within the department, and four internal email circulars to staff and students at King's College London. Interested volunteers were initially screened for eligibility against the inclusion criteria using a screening questionnaire administered by email or over the telephone. Potentially eligible participants were then invited to attend a screening visit at the Metabolic Research Unit located at the Franklin Wilkins Building, King's College London. After obtaining informed consent, participants were asked a series of questions to determine their self-reported disease and medication history. Measurements of BP, height, weight and waist circumference were made and fasting blood samples were taken to confirm that serum lipids (TC: HDL-C ratio <6.0 mmol/L, TGs <5.0 mmol/L, TC <8.0 mmol/L), haematology, liver function and glucose (<7.0 mmol/L) were within prescribed limits. A spot urine sample was collected to confirm non-smoking status by analysis of urinary cotinine, a metabolite of cigarette smoke that indicates an undisclosed smoking habit (current smoker indicated by cotinine >500 ng/L).

### **3.4.7 Randomisation**

Once eligibility had been confirmed, individuals were asked to complete two baseline measures of 24-hour ABP, two baseline 24-hour urine collections and a four-day food diary to provide an estimate of habitual dietary intake. Following collection of these baseline measures, a computerised minimisation programme was used to randomise participants to either the control or cardioprotective diet group. Data was entered onto a purpose-designed clinical database (MedSciNet AB, Stockholm, Sweden), which undertook the minimisation randomisation, balancing the treatment arms for the minimisation variables of gender (two groups: male and female), age (five groups 40-<50; 50-<55; 55-<60; 60-<65; 65- 70 years) and ethnicity (five

groups: white; black; South Asian, South East Asian and Middle Eastern; Far East; other). In the case where two partners living together were recruited to the study, both were allocated to the same treatment (n=17 couples).

### **3.4.8 Dietary intervention development**

Both the cardioprotective and control diet were developed to include foods that would be acceptable to participants, whilst meeting the nutrient and dietary targets. The cardioprotective diet aimed to meet multiple dietary targets (Table 3.3) and followed a systematic process as outlined in Full methods have been explained in detail in Chapter 2 (Section 2.2 Development of a cardioprotective dietary intervention). Practicalities and palatability were also considered in the strategies and final version of dietary advice developed. For the control diet, it was decided to compare the cardioprotective diet with a nutritionally balanced representative UK diet that would be acceptable to study participants and formulated with familiar foods (full cream milk, cheese, spreadable butter, meat and meat products, non-wholegrain cereals) which reflected typical intakes of fruit and vegetables (3 portions/day), had a higher SFA content (14% energy) than currently recommended, unrestricted intakes of salt and sugar and low intakes of oily fish. Both diets were intended to be isocaloric, and to provide 35% energy as fat.

### **3.4.9 Dietary intervention delivery**

Participants randomised to both of the diets were given individualised dietary advice to modify habitual intake to achieve the dietary targets. Written information (Appendix 3.1), which included food based guidance, advice on front of pack labelling, eating out and choosing convenience meals, was provided and verbally explained to each participant during the baseline visit. A selection of food products - common pantry items that are components of frequently consumed meals and recipes - was provided to allow ad libitum food consumption whilst maximising compliance to the food and nutrient targets. These products included vegetable oils and spreads, breakfast cereals, rice and pasta, tinned fish and baked beans, reduced salt and sugar sauces (cardioprotective diet group only) and snack foods. A similar strategy has been successfully used previously, but with a smaller number of dietary targets (Moore et al., 2009, Williams et al., 1999). The nutrient and food targets, and strategies used to maximise compliance, are summarised in Table 3.3.

Figure 3.1 Overview of methods used in the development of the cardioprotective dietary intervention based on UK dietary guidelines

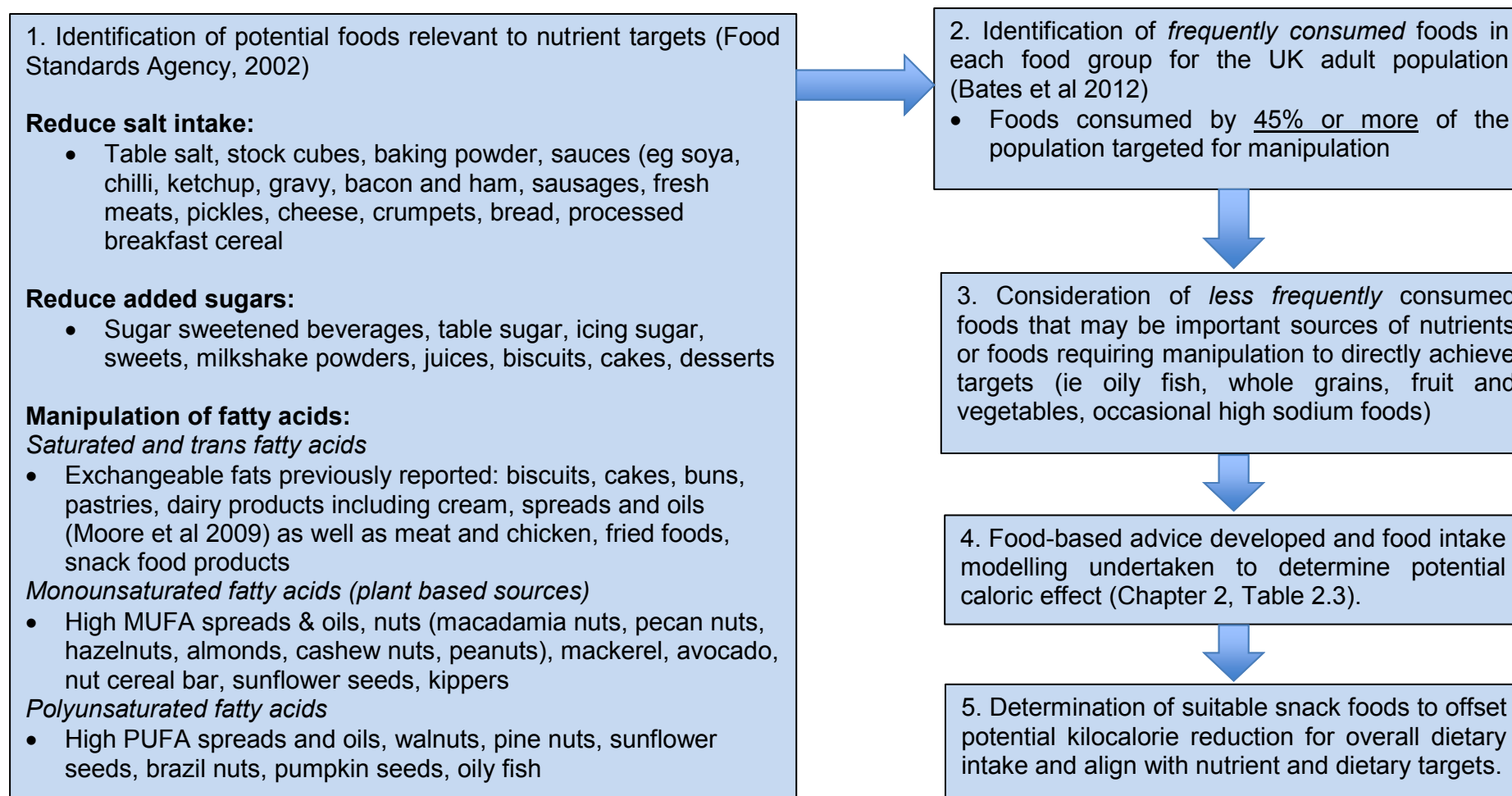


Table 3.3 Dietary targets and strategies adopted for CRESSIDA cardioprotective and control diets

	<b>Cardioprotective diet</b>	<b>Strategies used</b>	<b>Representative UK diet (control)</b>	<b>Strategies used</b>
<b>Salt</b>	< 6 g/ day	<p>Advised to cook using fresh ingredients that are naturally low in salt.</p> <p>Advised to avoid discretionary salt use (cooking, at the table).</p> <p>Advised to minimise intake of foods high in salt.</p> <p>Provision of reduced salt versions of condiments and tinned baked beans.</p>	Not restricted **	<p>No advice on salt.</p> <p>Provision of conventional tinned baked beans.</p>
<b>Saturated fatty acids</b>	< 10% energy	<p>Modified dietary fat exchange model (Moore et al., 2009) – provision of spread and oil. Advised to consume only the cooking oil and spreads provided.</p> <p>Advised to consume lean meat only, avoid processed meat products, replace red meat with skinless chicken or fish 2/week.</p> <p>Advised to consume low fat dairy products, restrict cheese, and avoid cream, biscuits, cakes.</p>	~ 14% energy	<p>Modified dietary fat exchange model (Moore et al., 2009) – provision of spread and oil. Advised to consume only the cooking oil and spreads provided.</p> <p>Advised to consume full fat dairy products, no restriction on cheese.</p>
<b>Fruit and vegetables</b>	5 portions/ day	Advised to consume five portions of a variety of fruit and vegetables each day, potatoes not included.	3 portions/ day	Advised to eat three portions of fruit and vegetables each day.



	Cardioprotective diet	Strategies used	Representative UK diet (control)	Strategies used
		<p>Specific portion guidance given for different types of fruit and vegetables.</p> <p>Fruit juice – advised to keep portion size small, counts as maximum one portion only.</p> <p>Discouraged consumption of fruit in syrup and vegetables in brine.</p>		
	<b>Oily fish</b>	2 portions/ week	<p>Reimbursement of costs for purchase of fresh oily fish.</p> <p>Provision of tinned oily fish.</p>	<p>Less than 1 portion/month</p> <p>Limit consumption of oily fish to one portion per month.</p> <p>Provision of tinned tuna.</p>
	<b>Whole grain</b>	> 50% cereal intake	<p>Provision of whole grain pantry items: whole meal pasta, microwaveable brown rice, choice of minimally processed whole grain breakfast cereals.</p> <p>Advice to consume whole grain bread.</p>	<p>Refined cereals</p> <p>Provision of refined cereal pantry items: white pasta and rice, choice of refined breakfast cereals low in whole grains.</p> <p>No advice on type of bread.</p>
	<b>Added sugars</b>	Restricted	<p>Advised to avoid sugar-sweetened beverages, avoid adding more than 4 teaspoons of sugar each day to tea/ coffee/ cereal.</p> <p>Advised to avoid biscuits, cakes, confectionary.</p>	<p>Not restricted **</p> <p>Advised to consume foods from the extras section of the Eatwell plate (Public Health England in association with the Welsh Government, 2013) in moderation and as occasional foods only.</p>

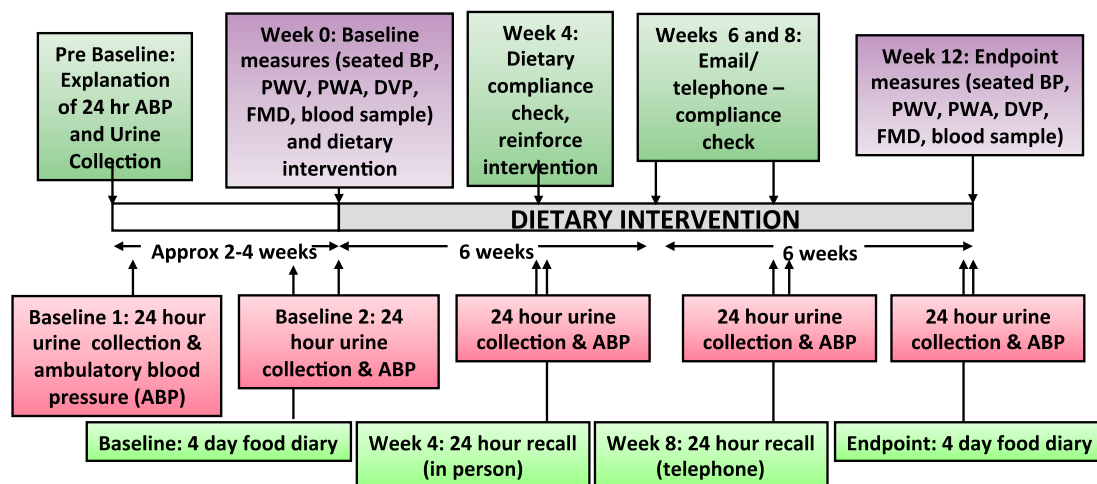
	<b>Cardioprotective diet</b>	<b>Strategies used</b>	<b>Representative UK diet (control)</b>	<b>Strategies used</b>
<b>Total fat</b>	~ 35% energy	Advised to daily consume 1-2 tablespoons of oil provided, and 2-4 teaspoons of spread provided.	~ 35% energy	Advised to daily consume 1-2 tablespoons of oil provided, and 2-4 teaspoons of spread provided

\*\* Not restricted: advice was aimed at maintaining intakes from baseline rather than encouraging increased intake of these foods.

### 3.4.10 Outcome measures

An overview of the study protocol is presented in Figure 3.2, including all visits and outcome measures undertaken.

Figure 3.2 Overview of participant visits and outcome measures during the 12 week intervention



Primary outcome measures were daytime SBP, TC:HDL-C and endothelial function. Systolic blood pressure, measured by 24-hour ABP monitoring, was chosen as it represents the most powerful predictor of cardiovascular risk (O'Brien et al., 2003); TC:HDL-C was chosen as the best available lipid indicator of risk (Lewington et al., 2007) and endothelial function, measured by flow mediated dilation, was chosen as an emerging and potentially important marker of risk. Outcome measures and time points are detailed in Table 3.4

Table 3.4 Cardioprotective dietary intervention study outcome measurements and time points

Outcome	Number of measures at each time point			
	Baseline <sup>1</sup>	Week 4	Week 8	Endpoint
<b>Primary</b>				
Systolic blood pressure measured by 24 hour ambulatory blood pressure monitoring	2	1	1	1
TC:HDL-C	1	-	-	1
Endothelial function measured by flow mediated dilation	1	-	-	1
<b>Secondary</b>				
Large artery function: carotid to femoral pulse wave velocity and stiffness index from the digital volume pulse	1	-	-	1
Resistance vessel function determined from the peripheral augmentation index based on the radial pulse waveform	1	-	-	1

<sup>1</sup>Baseline measures: where one baseline is indicated this was taken at week 0; where two baseline measures are indicated these were taken at weeks -2 and 0.

TC:HDL-C, ratio of total to high density lipoprotein cholesterol

### 3.4.11 Dietary monitoring and support

Participants from both the cardioprotective and control groups attended a follow up visit with the study dietitian within four weeks of commencing the allocated dietary intervention. At this visit, the dietitian checked each participant's understanding of the dietary advice provided at the baseline visit, conducted a 24 hour recall of foods eaten the previous day, re-measured the participant's weight and compared it to the individual's baseline weight, and provided suggestions for further dietary change or reinforced current dietary choices. At this visit, the second food delivery was also arranged which was delivered around week 6 of the intervention.

If participants had experienced a weight reduction of 1kg or more at the first visit they were provided with advice to promote weight stability. For example, where weight loss was identified, the participant was encouraged to ensure they ate the provided snacks daily, and given advice to increase the energy content of meals (liberal use of oil and spread provided, increased portion size, and more energy dense foods from the recommended foods to include) to prevent further weight loss. If weight gain was detected, advice to reduce higher calorie snacks and the energy content of meals (reduced portion size, less energy dense foods) was provided.

All participants were followed up by telephone again at week 6 and week 8. If weight was stable at the week 4 visit and participant understanding and compliance was acceptable, a follow up email was offered in place of the telephone call at week 6. For convenience, some participants opted for a face-to-face visit at week 8 (rather than a telephone call) to coincide with collection or return of BP equipment. In addition to formally scheduled visits, participants were also encouraged to contact the dietitian by phone or email if they had encountered problems following the advice, felt they were experiencing weight changes or required alternative or additional food products. No advice was given on physical activity, however physical activity was monitored via

a validated physical activity questionnaire administered at baseline and endpoint (Ekelund et al., 2006).

### **3.4.12 Dietary assessment**

Compliance to the allocated dietary intervention was assessed using estimated 4-day food records (one at baseline and one at endpoint). Nutrient intakes were estimated from the dietary records using NetWisp (version 3.0; Tinuviel Software, UK). Each individual's compliance to the dietary advice was also assessed twice during the intervention period using a triple pass 24 hour recall method (Nelson et al., 2007a) administered either in person (week 4) or by phone call (week 8). These were used to check the participant's understanding and reinforce the dietary advice provided at baseline. Full methods have been detailed in Chapter 2 (Section 2.3 Dietary Assessment Methods).

### **3.4.13 Data analysis**

#### **3.4.13.1 Data entry**

All measurement data was entered into a purpose built database (MedSciNet AB, Stockholm, Sweden) and checked for accuracy. The database included parameters to detect values outside of normal ranges, and automatically calculated a number of formulas including BMI (BMI), % FMD, % GTN, average of BP and arterial stiffness measurements to minimise human error. Data was directly exported from the database into spreadsheet format (Microsoft Corporation, Washington, USA).

#### **3.4.13.2 Statistical tests**

Data analysis was conducted in Stata version 11.1 (StataCorp, College Station Texas). Distributional checks for normality were undertaken, including the Kolmogorov-Smirnov test for normality and P-P plots. Where data did not conform to a normal distribution and was skewed, log transformations were performed as required and geometric mean with interquartile range (IQR) reported.

Results were summarised for each treatment group as mean (SD), n (%) or median (IQR) as appropriate. Comparison between randomised groups was based on an intention to treat basis. Data for all participants, once randomised, was included to the point of dropout and continued to be analysed as far as possible in their original randomised groups. Statistical analysis of the data was undertaken using ANCOVA which adjusted for baseline levels as well as regressing for the minimization variables used in randomization: age group, gender, BMI and ethnicity category. Treatment effects are shown as the comparisons between diets at the end of the study adjusted for baseline values.

Post-hoc average causal mediated effects analysis was undertaken to explore the effect of change in BMI on daytime SBP. Causal mediated effects analysis is routinely used by applied researchers to investigate alternative causal mechanisms for a difference in outcome between treatment groups (Imai, Keel & Yamamoto, 2010).

## **3.5 Results**

### **3.5.1 Baseline characteristics**

The CONSORT diagram (Figure 3.3) provides an overview of the flow of participants through the study. A total of 599 individuals enquired about the study and were provided with a Participant Information Sheet, from which 227 who appeared suitable attended a screening clinic to assess eligibility. Of these 165 were randomised to treatment and 162 completed the study. Reasons for non-completion were unrelated illness, family bereavement and unwillingness to follow dietary advice.

Participants randomised to each dietary group were similar at baseline (Table 3.5). There were more females than males, and about a fifth of participants were non-White. Participants were slightly overweight as indicated by the mean BMI, and the mean waist circumference was greater than the International Diabetes Federation recommendations of < 94cm for men and < 80cm for women (International Diabetes Federation, 2006). Blood pressure and TC:HDL-C were higher in men than women (data not shown). The majority of participants were employed in sedentary occupations and had completed some form of education above the age of 16 years (Table 3.6).

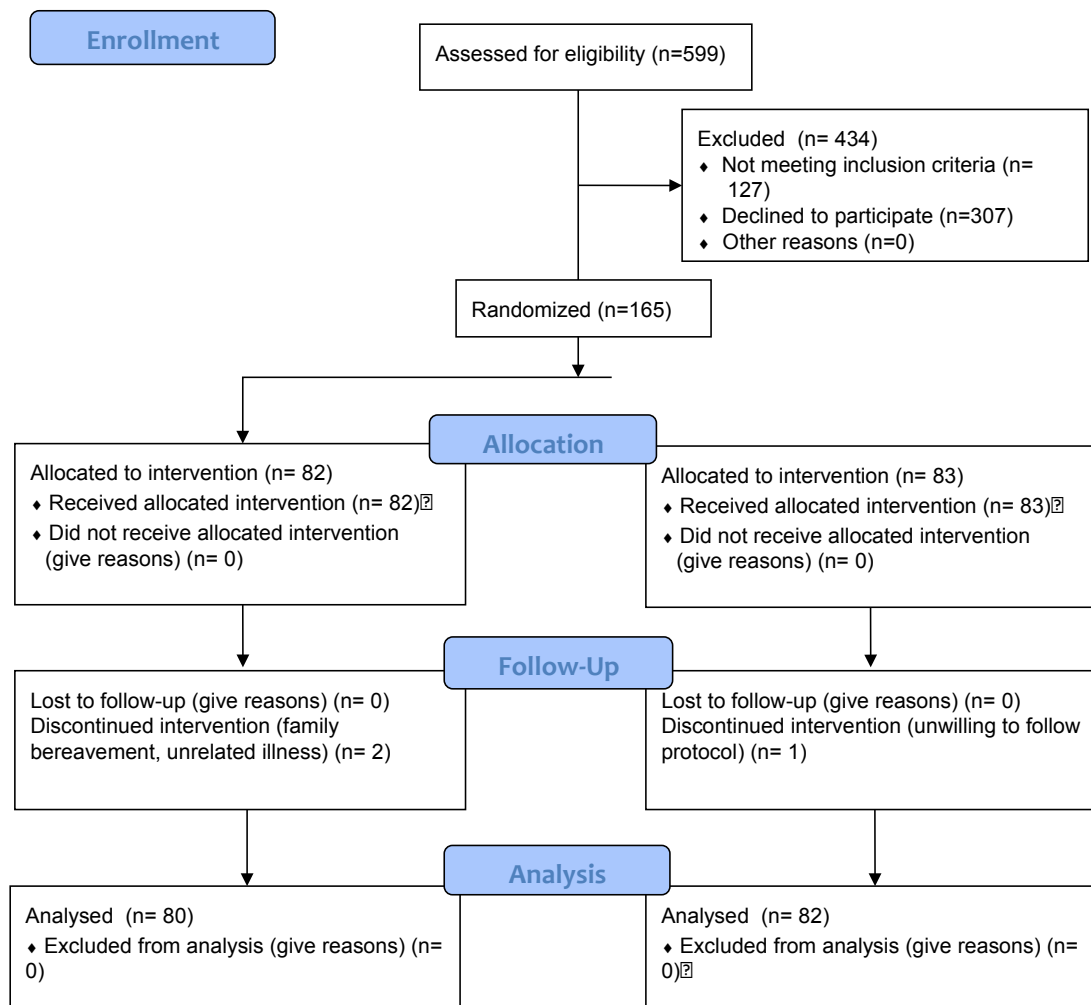


Figure 3.3 CONSORT flow diagram for participants in the CRESSIDA study

Table 3.5 Details of participants at baseline by randomised group

	<b>Cardioprotective Group n=82</b>	<b>Control Group n=83</b>	<b>P value</b>
<b>Age (years), Mean ± SD</b>	53 ± 8	52 ± 8	0.81
<b>Gender, N (%)</b>			
<b>Male</b>	32 (39.0)	33 (39.8)	
<b>Female</b>	49 (61.0)	50 (60.2)	
<b>Postmenopausal</b>	25 (50.0)	28 (56.0)	
<b>Ethnicity, N (%)</b>			
<b>White</b>	71 (86.6)	66 (79.5)	
<b>Black</b>	6 (7.3)	10 (12.0)	
<b>Asian<sup>1</sup></b>	2 (2.4)	7 (8.4)	
<b>Far Eastern</b>	2 (2.4)	0 (0.0)	
<b>Other</b>	1 (1.2)	0 (0.0)	
<b>BMI (kg/m<sup>2</sup>), Mean ± SD</b>	25.5 ± 3.7	26.8 ± 3.9	0.02
<b>Waist (cm), Mean ± SD</b>			
<b>Male</b>	98 ± 10	97 ± 12	0.79
<b>Female</b>	88 ± 12	91 ± 10	0.10
<b>SBP (mmHg), Mean ± SD</b>	119 ± 14	120 ± 14	0.15
<b>DBP (mmHg), Mean ± SD</b>	77 ± 8	79 ± 9	0.28
<b>Glucose (mmol/L)</b>	5.3 ± 0.5	5.2 ± 0.5	0.04
<b>TC:HDL-C, Mean ± SD</b>	3.5 ± 1.0	3.7 ± 1.0	0.30
<b>10 year risk of CVD (%)<sup>2</sup></b>			
<b>Male</b>	7.7 ± 5.2	7.6 ± 5.7	0.85
<b>Female</b>	3.3 ± 3.0	4.5 ± 3.5	0.07

<sup>1</sup>Asian= South Asian, SE Asian & Middle Eastern. <sup>2</sup>Q-RISK2 (Hippisley-Cox et al 2008)  
 SBP=seated systolic blood pressure, DBP= seated diastolic blood pressure,  
 TC:HDL-C=Ratio of total cholesterol to high density lipoprotein cholesterol



Table 3.6 Highest education achieved, employment status and most recent occupation category of all participants randomised

	Cardioprotective diet n=82	Control diet n=83
<b>Highest education achieved n (%)</b>		
None	6 (7.3)	6 (7.2)
CSE	6 (7.3)	6 (7.2)
GCE/O Level	11 (13.4)	14 (16.9)
A Level	3 (3.7)	5 (6.0)
HND, Diploma	6 (7.3)	6 (7.2)
NVQ & Professional qualification	7 (8.5)	4 (4.8)
Degree	30 (36.6)	30 (36.1)
Postgraduate qualification	15 (18.3)	14 (16.9)
Unknown	1 (1.2)	1 (1.2)
<b>Employment Status</b>		
Currently employed	62 (75.6)	55 (66.3)
Self-employed	3 (3.7)	1 (1.2)
Housewife/husband	2 (2.4)	3 (3.6)
Retired	10 (12.2)	10 (12.0)
Student	2 (2.4)	3 (3.6)
Unemployed/unwaged	1 (1.2)	9 (10.8)
Volunteer	1 (1.2)	2 (2.4)
<b>Office of National Statistics Occupation category<sup>1</sup></b>		
Professional	32 (39.0)	24 (28.9)
Managers, Directors & Senior Officials	10 (12.2)	8 (9.6)
Administrative And Secretarial	9 (11.0)	22 (26.5)
Associate Professional And Technical	9 (11.0)	12 (14.5)
Caring, Leisure And Other Service	9 (11.0)	5 (6.0)
Process, Plant & Machine Operatives	6 (7.3)	3 (3.6)
Sales And Customer Service	3 (3.7)	3 (3.6)
Elementary	3 (3.7)	3 (3.6)
Skilled Trades	0 (0.0)	3 (3.6)
Unknown	1 (1.2)	0 (0.0)

*Occupation category is the Office of National Statistics Major Group Category for each occupation.*

<sup>1</sup>*Includes most recent occupation of those that are not currently employed.*

## 3.5.2 Compliance with intervention

### 3.5.2.1 Nutrient intakes

Nutrient intakes at baseline and endpoint, derived from analysis of the 4-day food records, are presented in Table 3.7. Baseline nutrient intakes were similar between groups (no significant differences between groups; data not shown).

The cardioprotective diet group experienced reductions in mean total fat intakes compared to the control group. In particular, SFA intakes were lower, mostly compensated for by an increase in the proportion of fatty acids derived from MUFA and PUFA, with intakes of *n*-3 LCP increasing by 0.77 g/day. Dietary cholesterol intake was also reduced in the cardioprotective group. Mean protein intake, as a proportion of energy, was slightly higher in the cardioprotective group

compared to the control. There was no difference in total carbohydrate intake, but the intake of NMES was lower and dietary fibre intakes were higher in the cardioprotective group.

#### **3.5.2.2 Biomarkers of compliance**

A number of objective biomarkers of nutritional intake were measured as part of the larger cardioprotective dietary intervention study, but were not the focus of this thesis. For completeness, these results have been included in Appendix 3.2. Biomarkers for sodium, potassium, wholegrain and sugar intake were consistent with dietary changes indicated by the analysis of the 4-day dietary diaries.

#### **3.5.2.3 Body composition and physical activity**

Body weight decreased significantly in the cardioprotective group compared with the control group. There were concomitant reductions in BMI and waist circumference (Table 3.8). Self-reported levels of physical activity were low and did not change during the intervention period (Table 3.7).

Table 3.7 Nutrient intakes estimated from 4-day dietary diaries, physical activity level and BMI at baseline with changes following the cardioprotective and control diets

	Baseline		Endpoint		Between group comparison	<i>P</i> value**
	Cardioprotective n=80	Control n=82	Cardioprotective n=79	Control n=82		
	Mean $\pm$ SD* ( $p > 0.05$ between groups)		Mean change from baseline (95% CI)		Mean treatment effect (95% CI)	
Energy intake (MJ/d) <sup>†</sup>	8.97 $\pm$ 2.25	8.95 $\pm$ 2.49	-0.18 (-0.65, 0.31)	0.47 (-0.2, 0.97)	-0.59 (-1.18, 0.01)	0.052
Physical activity level <sup>‡</sup>	1.30 $\pm$ 0.15	1.30 $\pm$ 0.16	0.05 (-0.02, 0.13)	-0.03 (-0.10, 0.05)	0.08 (-0.02, 0.19)	0.125
Body mass index (kg/m <sup>2</sup> )	25.3 $\pm$ 3.6	26.9 $\pm$ 3.9	-0.4 (-0.6, -0.3)	0.2 (0.1, 0.3)	-0.7 (-0.9, -0.5)	<0.001
Protein (% energy)	16.0 $\pm$ 2.9	15.9 $\pm$ 3.2	1.8 (1.0, 2.4)	-0.2 (-0.9, 0.4)	2.1 (1.3, 2.9)	<0.001
Carbohydrate (% energy)	44.0 $\pm$ 6.9	45.7 $\pm$ 7.1	0.3 (-1.8, 1.1)	-1.8 (-3.2, 0.4)	0.5 (-1.2, 2.2)	0.578
Dietary fibre (g/d)	24.3 $\pm$ 8.6	23.5 $\pm$ 9.4	7.1 (5.1, 9.0)	-0.2 (-0.18, 1.5)	7.6 (5.2, 9.9)	<0.001
Sugars (% energy)	21.1 $\pm$ 6.1	20.8 $\pm$ 5.7	0.5 (-1.1, 2.2)	-0.6 (-2.0, 0.8)	0.9 (-1.1, 2.8)	0.385
NMES (% energy)	9.8 $\pm$ 4.3	9.9 $\pm$ 4.6	-2.5 (-3.7, -1.4)	-0.4 (-1.4, 0.6)	-2.6 (-3.7, -1.4)	<0.001
Fat (% energy)	36.0 $\pm$ 5.9	34.7 $\pm$ 6.2	-2.3 (-3.8, -0.8)	2.4 (0.8, 4.0)	-3.4 (-5.1, -1.7)	<0.001
SFA (% energy)	12.3 $\pm$ 3.5	11.6 $\pm$ 3.2	-4.7 (-5.5, -3.8)	3.2 (2.4, 4.0)	-7.2 (-7.9, -6.4)	<0.001
Trans fatty acids (% energy)	0.6 $\pm$ 0.3	0.6 $\pm$ 0.3	-0.4 (-0.4, -0.3)	0.2 (0.1, 0.3)	-0.6 (-0.7, -0.5)	<0.001
MUFA (% energy)	11.9 $\pm$ 2.5	11.8 $\pm$ 2.7	3.5 (2.7, 4.4)	0.5 (-0.2, 1.2)	3.3 (2.4, 4.3)	<0.001
PUFA (% energy)	6.6 $\pm$ 2.2	6.1 $\pm$ 1.7	0.6 (0.1, 1.2)	-0.8 (1.2, -0.3)	1.9 (1.3, 2.4)	<0.001
<i>n</i> -3 LCP (g/d)	0.2 $\pm$ 0.5	0.3 $\pm$ 0.8	1.2 (0.8, 1.5)	-0.3 (-0.5, -1)	1.3 (0.9, 1.7)	<0.001
Sodium (mmol/d)	140 $\pm$ 50	138 $\pm$ 56	-56 (-67, -45)	9 (-3, 22)	-65 (-78, -51)	<0.001
Potassium (mmol/d)	92 $\pm$ 25	90 $\pm$ 27	15 (10, 20)	1 (-3, 6)	12 (7, 20)	0.009

\*Baseline between group comparison for all variables  $p > 0.05$

\*\*Probability based on analysis of covariance with value on treatment regressed against the baseline value, age group, gender, ethnicity group and BMI category.

<sup>†</sup> Participants recording energy intake less than 1.2 x basal metabolic rate were excluded from estimates of energy intake; Baseline: Cardioprotective,  $n=18$ ; Control,  $n=25$ ; Endpoint: Cardioprotective  $n=23$ , Control  $n=20$ .

<sup>‡</sup> Physical activity level is the ratio of activity in relation to resting metabolic rate.

NMES, non-milk extrinsic sugars; SFA, saturated fatty acids; MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids; *n*-3 LCP, long chain *n*-3 polyunsaturated fatty acids.

Table 3.8 Body composition at baseline with changes following the cardioprotective and control diets

	Baseline*		Endpoint		Between Group Comparison <sup>†</sup>	P <sup>†</sup>
	Cardio-protective n=80	Control n=82	Cardio-protective n=80	Control n=82	Mean treatment effect (95% CI)	
Body weight (kg)	73.0 (14.0)	77.0 (13.5)	71.7 (13.2)	77.6 (13.8)	-2.0 (-2.6, -1.4)	0.0001
Waist circumference (cm)	91.1 (12.2)	94.2 (11.4)	90.6 (11.9)	95.2 (11.7)	-1.7 (-2.7, -0.6)	0.002

\*No significant differences at baseline, independent samples t-test <sup>†</sup>ANCOVA, adjusted for baseline value.

### 3.5.3 Outcomes

Primary outcomes were daytime SBP and TC:HDL and measures of endothelial function using the FMD technique. Secondary outcomes included large artery function using the pulse wave velocity (PWV) technique.

#### 3.5.3.1 Blood pressure

Mean baseline BP was similar between groups with no significant differences. The mean difference between groups in daytime systolic BP at endpoint, as measured by ABP, was 4.2 mmHg ( $P<0.001$ ). Statistically significant treatment effects were also seen with diastolic BP (-2.5 mmHg) and in night-time systolic and diastolic BP with a significantly reduced systolic/ diastolic BP of 3.5/2.2 mmHg with the cardioprotective dietary group compared to the control group (Figure 3.4; Table 3.9).

Causal mediated effects analysis indicated that the effect of change in BMI contributed around 31% of the difference in endpoint SBP between groups, suggesting that a 0.7 kg/m<sup>2</sup> difference in BMI would account for a mean (95% CI) of -1.2 (-2.6 to 0.01) mmHg of the difference in daytime SBP between groups.

#### 3.5.3.2 Blood lipids

Mean baseline TC:HDL-C, total, HDL-, LDL- cholesterol and triglycerides were similar with no significant differences between groups. Following the intervention, the mean TC:HDL-C was 4.2% lower in the cardioprotective group compared to the control group ( $P=0.044$ ; Table 3.10). The change in apoB:apoA1 was in the same direction ( $P=0.04$ ). Serum TGs and total, LDL and HDL cholesterol were lower on the cardioprotective diet compared with the control diet (Table 3.10).

### **3.5.3.3 Endothelial function**

Baseline flow FMD and endothelium independent vasorelaxation induced by GTN were similar between groups, with no significant differences. Changes in endothelial function, as measured by FMD, were small and not significant (Table 3.11). There were no differences in response between male and female, or premenopausal and postmenopausal participants by treatment. There was no evidence of change in endothelium independent vasorelaxation induced by GTN. 1.1.1.1 Vascular function

### **3.5.3.4 Vascular function**

Table 3.12 shows the treatment effect on measures of arterial stiffness, augmentation index, digital volume pulse measures, supine central BP and heart rate. PWVc-f was 0.29m/sec (95% CI 0.07, 0.052; P=0.011) lower, and after adjusting for central mean arterial pressure, a difference of 0.19 m/sec (95% CI 0.10, 0.28; P<0.001) remained. The lower supine central systolic/diastolic BP was 3.5/2.4 mmHg compared to the control group corresponded with the change in 24 hour BP. There were no changes in augmentation indices or measures of digital volume pulse (DVP). Heart rate was 1.8 beats per minute lower.

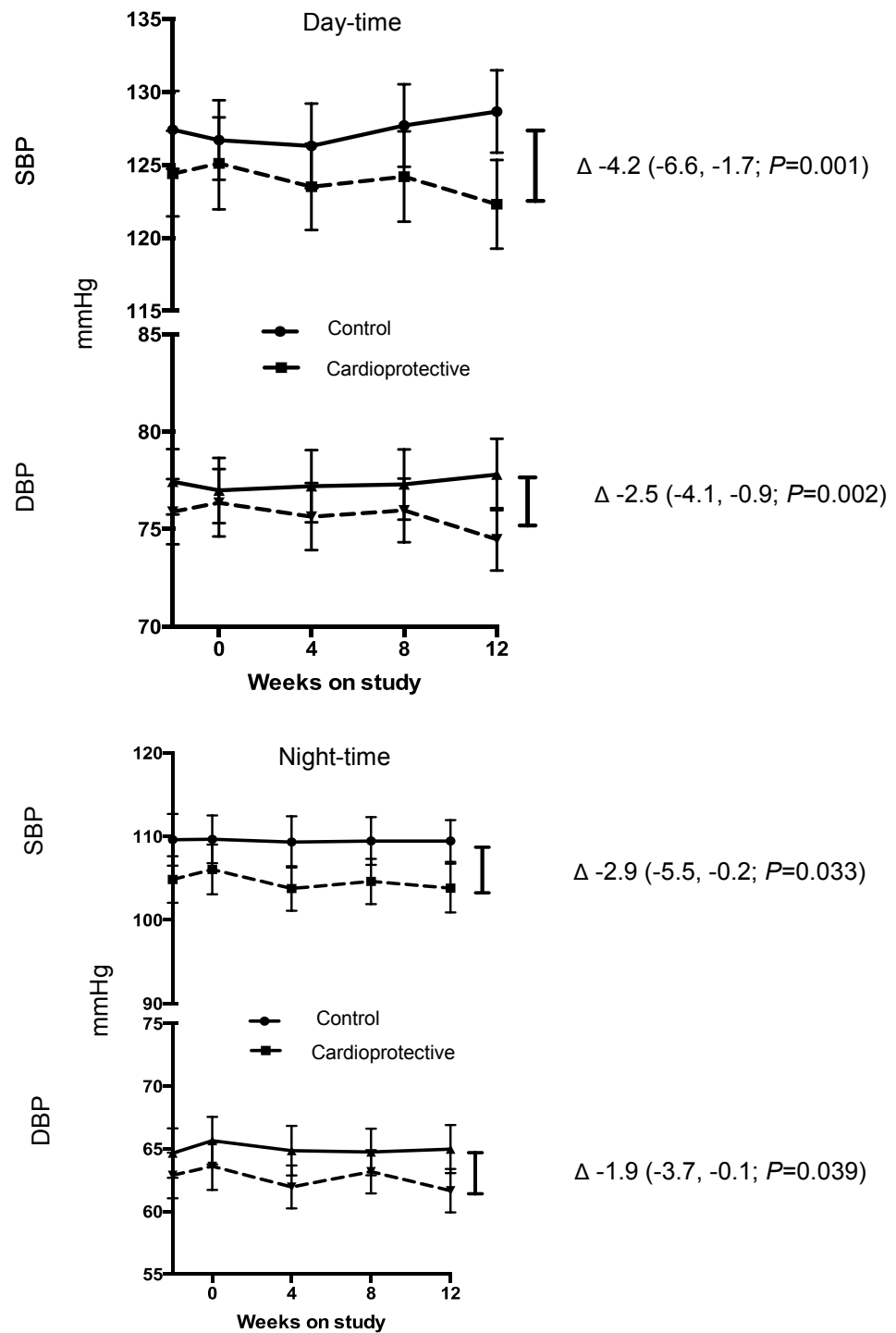


Figure 3.4

Change in day time (upper panel) and night time (lower panel) ambulatory blood pressure. Values are mean with 95% CI. SBP, systolic blood pressure; DBP, diastolic blood pressure; CI, confidence interval;  $\Delta$ , mean change adjusted for baseline value.

Table 3.9 Ambulatory blood pressure before, during and after treatment

	Cardioprotective		Control		Between Group Comparison (95% CI)	P*
<b>Daytime Systolic BP (mmHg)</b>						
Baseline 1	N=81	124.16 (13.14)	N=83	127.36 (12.10)		
Baseline 2	N=81	125.22 (14.05)	N=83	126.71 (12.46)		
Mean baseline	N=81	124.69 (13.06)	N=83	126.04 (11.41)		
Week 4	N=78	123.49 (13.16)	N=79	126.30 (12.96)		
Week 8	N=78	124.17 (13.72)	N=80	127.68 (12.68)		
Endpoint	N=80	122.34 (13.55)	N=80	128.65 (13.10)	-4.16 (-6.66 to -1.65)	0.001
<b>Daytime Diastolic BP (mmHg)</b>						
Baseline 1	N=81	75.89 (7.56)	N=83	77.43 (7.66)		
Baseline 2	N=81	76.35 (7.78)	N=83	76.98 (7.64)		
Mean baseline	N=81	76.12 (7.26)	N=83	77.20 (7.20)		
Week 4	N=78	75.64 (7.66)	N=79	77.04 (8.27)		
Week 8	N=78	75.96 (7.25)	N=80	77.29 (8.08)		
Endpoint	N=80	74.47 (7.17)	N=80	77.80 (8.22)	-2.48 (-4.07 to -0.89)	0.002
<b>Night time Systolic BP (mmHg)</b>						
Baseline 1	N=81	104.84 (12.59)	N=82	109.60 (14.08)		
Baseline 2	N=81	106.04 (13.47)	N=83	109.65 (13.01)		
Mean baseline	N=81	105.44 (12.31)	N=83	109.60 (11.99)		
Week 4	N=78	103.76 (11.82)	N=79	109.33 (13.70)		
Week 8	N=77	104.60 (11.97)	N=80	109.45 (12.82)		
Endpoint	N=80	103.81 (12.51)	N=80	109.41 (11.20)	-2.86 (-5.48 to -0.24)	0.03
<b>Night time Diastolic BP (mmHg)</b>						
Baseline 1	N=81	62.88 (8.22)	N=82	64.65 (8.95)		
Baseline 2	N=81	63.60 (8.53)	N=83	65.65 (8.67)		
Mean baseline	N=81	63.24 (7.75)	N=83	65.16 (7.76)		
Week 4	N=78	61.95 (7.58)	N=79	64.85 (8.83)		
Week 8	N=77	63.17 (7.61)	N=80	64.74 (8.35)		
Endpoint	N=80	61.65 (7.79)	N=80	64.97 (8.63)	-1.91 (-3.72 to -0.10)	0.04

	Cardioprotective		Control		Between Groups Comparison Mean difference (95% CI)	P*
24h Systolic BP (mmHg)						
Baseline 1	N=81	119.91 (12.50)	N=83	123.57 (11.91)		
Baseline 2	N=81	120.96 (13.50)	N=83	122.69 (12.25)		
Mean baseline	N=81	120.44 (12.59)	N=83	123.13 (11.26)		
Week 4	N=79	119.25 (12.48)	N=79	122.25 (12.21)		
Week 8	N=77	119.68 (12.83)	N=80	123.97 (12.11)		
Endpoint	N=80	118.40 (12.83)	N=80	124.03 (11.79)	-3.47 (-5.72 to -1.22)	0.003
24h Diastolic BP (mmHg)						
Baseline 1	N=81	73.01 (7.34)	N=83	74.60 (7.28)		
Baseline 2	N=81	73.49 (7.55)	N=83	74.28 (7.52)		
Mean baseline	N=81	73.25 (7.14)	N=83	74.44 (7.01)		
Week 4	N=79	72.73 (7.12)	N=79	74.27 (7.79)		
Week 8	N=77	73.03 (6.86)	N=80	74.84 (8.17)		
Endpoint	N=80	71.78 (6.81)	N=80	74.78 (7.90)	-2.21 (-3.62 to -0.79)	0.002

Values are mean (SD) except for between group comparison which are presented as mean (95% CI).

\*Estimates, confidence intervals, and P-value are based on analysis of covariance adjusted for baseline level and for age group, gender, ethnicity and BMI category.



Table 3.10 Changes in serum lipid, apolipoprotein B and A1 concentrations following cardioprotective or control diet

	Baseline*		Endpoint		Between Group Comparison	P <sup>†</sup>
	Cardioprotective n=82	Control n=83	Cardioprotective n=80	Control n=82	Mean difference (95% CI)	
TC:HDL-C	3.46 (0.91)	3.63 (0.98)	3.31 (0.87)	3.59 (0.96)	-0.13 (-0.26, -0.00)	0.044
Total Cholesterol (mmol/L)	5.33 (1.11)	5.35 (0.86)	5.06 (0.93)	5.49 (0.89)	-0.46 (-0.64, -0.28)	<0.0001
LDL-Cholesterol (mmol/L)	3.18 (0.89)	3.18 (0.77)	3.00 (0.75)	3.29 (0.78)	-0.30 (-0.43, -0.17)	<0.0001
HDL-Cholesterol (mmol/L)	1.61 (0.40)	1.56 (0.42)	1.58 (0.38)	1.62 (0.44)	-0.10 (-0.17, -0.03)	0.005
Apolipoprotein B (g/L)	0.96 (0.25)	0.99 (0.22)	0.92 (0.21)	1.00 (0.22)	-0.065 (-0.098, -0.032)	0.0002
Apolipoprotein A1 (g/L)	1.57 (0.31)	1.55 (0.30)	1.55 (0.33)	1.57 (0.30)	-0.043 (-0.090, -0)	0.035
Triglycerides (mmol/L)	1.24 (0.59)	1.33 (0.58)	1.06 (0.45)	1.23 (0.55)	-0.12 (-0.23, -0.01)	0.027

Values are mean (SD) except for between group comparison which are presented as mean (95% CI).

\*No significant difference between groups at baseline. <sup>†</sup>Probability of treatment effect from analysis of covariance regressed against age, BMI, ethnicity, gender and baseline value.

TC:HDL-C, ratio of total cholesterol to HDL cholesterol; LDL: low density lipoprotein; HDL: high density lipoprotein

Table 3.11 Changes in endothelium dependent (FMD) and independent (GTN) responses of the brachial artery following cardioprotective or control diet

	Baseline*		Endpoint		Between Group Comparison	P <sup>†</sup>
	Cardioprotective	Control	Cardioprotective	Control	Mean difference (95% CI)	
<b>FMD (%)<sup>‡</sup></b>	5.61 (3.00)	5.33 (3.24)	4.94 ± 2.54	5.44 ± 3.30	-0.62 (-1.48, 0.24)	0.16
<b>GTN (%)<sup>§</sup></b>	11.27 (4.83)	10.63 (4.94)	11.78 ± 5.63	10.98 ± 4.24	0.17 (-1.20, -1.53)	0.80

Values are mean (SD) except for between group comparison.

FMD=flow mediated dilation; GTN= glycerol trinitrate wave velocity.

\* No significant differences at baseline. <sup>†</sup> Probability of treatment effect from analysis of covariance regressed against age, BMI, ethnicity, gender and baseline value

<sup>‡</sup> Cardioprotective, n=73; Control, n=76. <sup>§</sup> Cardioprotective, n=72; Control, n=76.

Table 3.12 Supine clinic blood pressure, supine heart rate, carotid-femoral pulse wave velocity (PWV<sub>c-f</sub>), aortic and peripheral augmentation index (AI),

	Baseline				Endpoint				Between Group Comparison Mean difference (95% CI)	P*
	n	Cardioprotective	n	Control	n	Cardioprotective	n	Control		
<b>Central SBP (mmHg)</b>	81	109.1 (13.8)	82	109.9 (12.4)	80	105.0 (11.6)	82	109.4 (12.4)	-3.5 (-5.4, -1.6)	<0.001
<b>Central DBP (mmHg)</b>	81	75.1 (8.1)	82	75.7 (8.5)	80	72.2 (7.3)	82	75.5 (8.8)	-2.4 (-3.8,-1.1)	0.001
<b>Central MAP (mmHg)</b>	81	89.8 (9.9)	82	90.7 (10.0)	80	86.3 (8.6)	82	90.4 (10.0)	3.0 (-4.5,-1.5)	<0.001
<b>Heart rate (bpm)</b>	81	57.5 (7.4)	82	57.1 (8.3)	80	55.2 (7.7)	82	57.8 (9.2)	-1.8 (-3.3, -0.3)	0.022
<b>PWV<sub>c-f</sub> (m/sec)</b>	80	7.65 (1.31)	83	7.39 (1.09)	78	7.43 (1.22)	81	7.61 (1.14)	-0.29 (-0.52,-0.07)	0.011
<b>Aortic AI (%)</b>	81	17.2 (9.7)	81	19.1 (9.9)	78	16.4 (9.5)	80	19.6 (10.4)	-1.2 (-2.7, 0.3)	0.115
<b>Peripheral AI (%)</b>	81	79.4 (14.9)	82	81.5 (13.5)	80	78.3 (14.4)	82	81.4 (14.7)	-0.6 (-3.1,1.9)	0.616
<b>DVP<sub>RI</sub> (%)</b>	77	64.9 (14.6)	80	65.1 (16.0)	74	68.0 (15.5)	76	66.2 (16.0)	1.1(-3.1,5.3)	0.607
<b>DVP<sub>SI</sub> (%)</b>	77	6.2 (1.8)	80	6.6 (2.2)	74	6.9 (2.2)	76	7.1 (2.7)	-0.2(-1.0, 0.48)	0.520

digital volume pulse reflection index (DVP<sub>RI</sub>) and stiffness index (DVP<sub>SI</sub>)

Mean values (SD).

SBP=systolic blood pressure, DBP=diastolic blood pressure, MAP=mean arterial pressure

\*Estimates with 95% confidence intervals and P-value are adjusted for baseline level and for age group, gender, ethnicity and BMI.

### 3.6 Discussion

This study set out to investigate the effect of a cardioprotective dietary pattern on CVD risk factors, compared with one typically consumed in the UK as a control. Participants were middle aged, with characteristics similar to those described in the Health Survey for England: overweight, with a waist circumference greater than recommended, and a slightly elevated TC:HDL-C; however SBP was slightly lower than mean values reported in the most recent NDNS (Public Health England and Food Standards Agency, 2014) - although the NDNS used a single clinic BP measure only. The results showed an effect of the cardioprotective diet on two of the primary outcomes, with a significant reduction in daytime SBP of 4.2 mmHg and a 4.2% reduction in TC:HDL-C compared to the control diet. As well as the reduction in SBP, there was a significant decrease in overall 24-hour ABP of 3.5/2.2 mmHg. Night time BP was also 2.9/1.9 mmHg lower in the cardioprotective group compared to the control group. The reductions in BP were accompanied by improvements in arterial stiffness in the cardioprotective group, as measured by PWVc-f.

Participants' dietary intakes at baseline were broadly similar to those reported in the NDNS for saturated fat, salt and sugar intakes. However intakes of wholegrain cereals, fruit and vegetables were higher than the general population (Public Health England and Food Standards Agency, 2014). Analysis of the dietary records suggested that during the intervention the majority of dietary targets were met by the cardioprotective group, including a reduction in the proportion of energy from SFAs (7.7% energy from saturated fat achieved against a target of 10%), an increase in the number of portions of fruit and vegetables consumed per day (up from around 5 to a mean of 7 per day), an increase in portions of oily fish consumed (increased from less than 1 portion per week to a mean of 1.7 portions per week), an increase in the proportion of whole grain cereals consumed (to around 75% of all cereals eaten) which was accompanied by a concomitant increase in non starch polysaccharides (which increased from a mean of 17g per day to a mean of 22g per day), and a reduction in intake of added sugars (although mean total sugars did not change, this was likely due to an increase in dietary sugar from fruit).

Although not the focus of this thesis, urinary excretion of sodium in the cardioprotective diet group fell from baseline values, supporting the dietary records which suggested a difference in sodium intake of 65 mmol/day per day - equivalent to around 3.8g salt per day. Urinary excretion in the cardioprotective group was equivalent to a mean intake of around 5.4g salt per day (against a target of less than 6g/day). Other biomarkers of compliance supported the dietary records, with a small increase in potassium excretion, an increase in *n*-3 LCP in erythrocyte lipids, an increase in plasma alkylresorcinols (accompanied by a reduction in serum folate, reflecting a reduced intake of refined cereals fortified with folic acid) and a reduction in urinary sucrose and fructose.

The proportion of energy derived from protein increased slightly in the cardioprotective group when compared to the control group because of advice to remove dietary fat from animal products (predominantly dairy and meat). In absolute terms the difference in protein intake was small, about 4g/d between the two groups and was not statistically significant. The control diet was

nutritionally balanced and differed little from the participants' usual diet besides the slightly higher intake of saturated fat (8 g/d).

The reduction in daytime SBP of 4.2mmHg demonstrates the impact of the dietary intervention on blood pressure even in participants who are normotensive. The effect is comparable to the DASH dietary intervention trial, where the combination dietary pattern achieved a mean reduction in systolic blood pressure of 5.5 mmHg. However mean blood pressure of participants in that trial was in the pre-hypertensive range, and the results showed that those in the hypertensive category experienced greater reductions in blood pressure than those participants in the pre-hypertensive category (Appel et al 1997). In terms of SBP, between the ages of 40-69 years a difference of 20 mmHg is associated with a doubling of risk of death due to ischaemic heart disease (IHD), with the same proportional difference in risk down to at least 115 mmHg (Lewington et al., 2002). The genesis of hypertension occurs over many years and it is a self-amplifying condition. Consequently, the effects of a similar population-wide intervention to lower BP has the potential for a greater public health impact than focusing on those with hypertension alone. The Lewington review results suggest that the public health significance of achieving similar reductions in blood pressure in the UK population would equate to a reduction in the risk of heart attack and stroke by 17% and 20% respectively (Lewington et al., 2002).

Endothelial function, as measured by FMD, did not differ between groups. This was in contrast to previous short-term studies (ranging from a single meal post-prandial effect to a duration of 2 weeks) which have suggested that a reduction in salt intake might improve endothelial function (Dickinson et al., 2009, Dickinson et al., 2011) however the results did not support this. This is likely to be because the current investigation was of a larger number of participants compared to previous studies (Dickinson et al., 2011, Dickinson et al., 2009) (which were n=16 and n=29 respectively) and the reduction in sodium intake was less pronounced: mean sodium intake fell from just under 150mmol/day to 93 mmol/day compared with a reduction from 150 mmol/day to 50 mmol/day in the Dickinson study (Dickinson et al., 2009). Aside from sodium reduction, the effect of n-3 LCP in amounts similar to those achieved in the current study did not have an impact on endothelial function in the MARINA study (Sanders et al., 2011). There are fewer studies investigating the longer term impact of dietary fat on endothelial function (Hall, 2009) and these results suggest there is no effect on endothelial function in a healthy middle aged population.

Compared to the control group, there was a modest reduction in weight in the cardioprotective group of just under 2kg (resulting in a mean 0.7 kg/m<sup>2</sup> lower BMI in the cardioprotective group compared to the control group). This weight change occurred spontaneously and despite dietary advice encouraging isocaloric intake and the provision of snacks to meet the expected reduction in energy intake associated with the dietary changes to meet the saturated fat and sugar targets. Reported energy intakes, from four-day food diaries at baseline and endpoint, were lower in the cardioprotective group (but did not reach significance) and physical activity levels did not appear to increase. Similar weight changes occurred with isocaloric controlled feeding in the DASH study (-0.4kg in 4 weeks) (Appel et al., 1997) and with ad libitum self selected food intake intended to promote weight loss where BMI was > 25 kg/m<sup>2</sup> in the PREMIER study (-5.8kg in 6 months) (Appel et al., 2003). The results of causal mediated effects analysis indicated that around a third

of the effect on daytime systolic blood pressure could be explained by the change in BMI which occurred during the intervention. Of note, daytime SBP change did not change from baseline in the control group.

As noted, the mean ratio of TC:HDL-C was 4.2% lower in the cardioprotective group, a result which reached statistical significance. There was an 8.1% reduction in total cholesterol, which was accompanied by a 10% reduction in LDL-C concentrations in the cardioprotective group, compared to the control group. Whilst both total and LDL cholesterol were reduced in the cardioprotective group, there was a less favourable concurrent 6.2 % reduction in HDL cholesterol. Overall, the TC:HDL-C between groups favoured the cardioprotective dietary group. Total to HDL-cholesterol is a powerful lipid predictor of cardiovascular risk (Stampfer et al., 1991), and it has been estimated that a 1.33 unit increase in the ratio increases risk of death from IHD by a third (Lewington et al., 2007). Thus, similar reductions on a population basis in the UK has the potential to achieve a significant public health impact.

The difference in lipids between the groups at endpoint were all positive, except for the reduction in HDL cholesterol in the cardioprotective group compared to the control group. There are a number of dietary factors believed to affect HDL cholesterol that may explain the reduction observed, including macronutrient composition, change in intake of omega-3 fatty acids and weight loss. Manipulation of the macronutrient composition of the diet is known to have an effect on HDL-C. In the current study, carbohydrate as a proportion of total energy intake was unchanged between groups from baseline to endpoint. However the proportion of energy derived from total fat was slightly reduced in the cardioprotective group, and the proportion from protein was slightly higher. In addition, there was a reduction in the proportion of energy from SFA, which was accompanied by an increase in MUFA and PUFA, including an increase in intakes of *n*-3 LCP. Although *n*-3 LCP is thought to have a neutral effect on HDL-C, and theoretically the replacement of SFA with PUFA as well as MUFA should have favoured a stable HDL-C, the reduction in total fat and subsequent serum total cholesterol falls have likely also resulted in concomitant reductions in HDL-C. The between-group comparison with the control group, whose total cholesterol and HDL-C both rose slightly at endpoint, has an additive effect on the treatment difference.

It is possible that the small reduction in weight in the cardioprotective group also had a negative impact on mean serum HDL cholesterol levels. In a meta-analysis (Dattilo and Kris-Etherton, 1992) on the effect of weight reduction on HDL-C, studies where participants were actively reducing weight showed a reduction in HDL-C of around 8%. However pooled results of studies where participants were at a stabilised, yet reduced, weight showed an increase in serum HDL-C (Dattilo and Kris-Etherton, 1992). Thus one other possibility is that the reduction in HDL-C observed in the current study may have been a short-term effect, as it occurred at the same time as a small but significant reduction in weight in the cardioprotective group.

These results are modest but important because they occurred in a population of older adults described as of moderate risk rather than high risk. It has previously been estimated that around a third of cardiovascular events occur in those in the non-hypertensive range (Stamler et al., 1993). The present study did not exclude individuals on the basis of BP below any threshold and as such

demonstrates the effects of an integrated dietary approach across the range of normal BP in the non-medicated population. Similar dietary pattern research (for example the DASH and PREMIER studies (Appel et al., 1997, Sacks et al., 2001)) targeting high-risk individuals (hypertensive and pre-hypertensive) have demonstrated an effect of diet on BP as well as blood lipids (Harsha et al., 2004), and diet has frequently been proposed as a strategy to reduce CVD risk using a whole of population approach (Appel et al., 2006, Stamler et al., 1993). However to date there has been no strong or direct evidence of influence on risk in non-hypertensive middle aged adult populations.

### **3.7 Strengths and limitations of the study**

The main strength of this study was that it was conducted in a free-living population of people whose risk factors, except for their age, would not otherwise put them at high risk of CVD. They were not on lipid or BP lowering medication. Although participants were healthy, their intakes of total fat, SFAs, sugar and salt were similar to the general UK population.

Participants were able to freely choose the foods they ate during the study which strengthens the generalizability of the findings, compared to controlled feeding trials which are less transferable to real world settings. The measures of objective dietary biomarkers showed good compliance and corroborated dietary records, which indicated that the participants followed the dietary advice provided. The results demonstrate that an integrated dietary approach to CVD prevention in this population is both possible and effective in reducing cardiovascular risk.

The study also had a number of limitations, which should be noted. The duration of dietary change was relatively short term, and it is unknown whether the changes could be sustained beyond the intervention period of three months (nor whether risk factor changes would persist). Participants were volunteers who were motivated and expected to be asked to make dietary changes for a relatively short period of time, which may have made them more likely to change their diet than a non-volunteer being asked to make long term changes to the food they ate. Whilst the provision of study foods and regular follow up by a dietitian helped participants to comply with the dietary changes requested, such assistance would not usually be provided to healthy people in a non-study environment.

Although designed to be isocaloric, there was a small but statistically significant reduction in weight in the cardioprotective dietary group compared to the control group. A Cochrane review on the effect of weight loss on blood pressure in people with hypertension concluded that weight loss in the range of 4-8% was associated with a reduction in blood pressure of around 3mmHg systolic and diastolic. This suggests that the weight loss in the current study of normotensive people is likely to have made a contribution to the reduction in blood pressure in the cardioprotective group compared to the control group. It is possible that the reduction in weight, which occurred spontaneously in people who were overweight, may be an unavoidable consequence of following a diet consistent with the UK dietary guidelines.

Although well received in this population of motivated volunteers to a dietary intervention study, the demographics are not representative of the wider UK population. Participants were

predominantly White, well educated, and employed in professional or semi-professional roles and therefore likely to have been at lower risk of CVD events than more disadvantaged groups. People employed in 'high strain' jobs (characterised by high demands but low job control) are known to be at higher risk of CVD events, even where risk factors are not increased, than those in lower strain jobs (Nyberg et al., 2013). It is likely to be a greater challenge to bring about similar dietary changes in people on lower incomes, those who are less educated and those lacking skills and household infrastructure to purchase, store and prepare foods as recommended (Caraher et al., 1998, Preston and Rajé, 2007). Public health interventions that tackle these wider determinants of health are likely to be needed to successfully bring about dietary changes in populations from lower socioeconomic backgrounds (Di Cesare et al., 2013).

### **3.8 Conclusion**

A cardioprotective dietary pattern consistent with the UK dietary guidelines was successfully implemented in the cardioprotective dietary group for 12 weeks. Compared to the representative UK dietary group, this group experienced a reduction in daytime SBP and TC:HDL-C but no improvement in endothelial function healthy adults aged 40 to 70 years. The population impact of these changes in the primary outcomes, as assessed by evaluating meta-analyses examining changes in risk associated with change to BP and serum cholesterol levels, suggest that if the CRESSIDA cardioprotective dietary pattern was to be implemented across the whole of the UK population, the combined effects from the primary outcomes would have the potential to lower CVD rates in the UK by about a third.

## **Chapter 4 Exploring barriers, motivators and enablers to dietary change: a qualitative study**

### **4.1 Introduction**

Diet and lifestyle have been identified as behaviours which could have a major impact on the health of the UK population (National Institute for Health and Care Excellence, 2007). These behaviours are deeply influenced by an individual's social, cultural and material circumstances (Marmot et al., 2008). The Wanless Report called for a public health system where people are "fully engaged" and supported in making individual choices that collectively shift the social norms of behaviour. It identified that although there is often good scientific evidence for interventions, there is a paucity of information on the practical implementation of evidence-based prevention activities (Wanless, 2004). Building on existing publically funded research activities to engage individuals and evaluate behaviour change processes has the potential to improve the transferability of scientifically based interventions at very little additional cost.

### **4.2 Implementing intervention-based studies in real world settings**

Qualitative research can provide important insights into the context and process of an intervention from a service user perspective, and is a useful adjunct to quantitative evaluation methods which may not reflect the experience of the participants in the intervention being evaluated (Craig et al., 2006). Understanding the context of the original intervention is crucial, as interventions that may be effective in one context may not be effective in others. Whilst trials of efficacy shun variation, it may be much more accepted in effectiveness trials which may be deliberately designed to be tailored to different population groups and segments of the community. Practitioners looking to implement evidence-based interventions may need to adapt the intervention for translation to the community (National Institute for Health and Care Excellence, 2007).

Concordance with behaviour change to reduce risk factors for disease, framed using the Health Belief Model, emphasises a number of conditions that influence an individual's adoption of a health behaviour. These factors include the right cues to action, the individual's perceived vulnerability to the problem being addressed, the seriousness of the illness in the mind of the individual, the perceived effectiveness of the action in addressing the problem and the perceptions of the costs of adopting the treatment or action (Becker and Maiman, 1980, Chatterjee, 2006). An examination of the experience of research participants in relation to each of these factors may be useful for those interested in implementing evidence based interventions in real world settings.

Whilst there are extensive quantitative reports of dietary interventions including examples of robust objective measures of dietary compliance, there is less reported about the experiences of people undergoing the process of behaviour change within a complex intervention targeting diet. The Oslo Study Diet and Anti-Smoking Trial used focus groups to explore the experience of behaviour change for high risk participants who were receiving an intervention to improve diet and



to stop smoking over a period of more than ten years (Cable et al., 1999). The study intervention was very similar to clinical practice, and the focus groups highlighted a strong doctor-patient relationship, significant others, motivators, barriers and empowerment as important themes (Cable et al., 1999). Although qualitative in nature, the methodology adopted makes it more of a descriptive study than a coherent, theoretically driven conceptual study that is the preferred methodology for qualitative research (Gibbs et al., 2007). Such studies are still valuable, providing a rich complement to the quantitative data collected and proposing insights into the complex influences on food choice behaviour (Swift and Tischler, 2010). Using qualitative methods to complement quantitative nutrition research in this way is an important step to bridge the research-practice gap.

### **4.3 Aim of the research**

In order to understand dietary behaviour change more fully, and to guide the translation of the intervention to practice settings, this research aimed to explore the experiences of participants who had been randomised to the cardioprotective diet arm of the Cardiovascular risk REduction Study: Supported by an Integrated Dietary Approach (CRESSIDA study <http://www.controlled-trials.com/ISRCTN92382106>) which recruited healthy people aged 40-70 years.

The objectives were:

1. To explore participants' perception of barriers, reinforcing and enabling factors influencing dietary change consistent with the UK dietary guidelines.
2. To explore participants' perception of the advantages and disadvantages of following the dietary guidelines.

### **4.4 Methods**

#### **4.4.1 Study design and overview**

This was a qualitative study using semi-structured 1:1 interviews with a sample of participants randomised to the cardioprotective diet group of the CRESSIDA study. Face to face interviews were conducted to explore participants' experiences during the twelve-week dietary intervention. Thematic analysis was used to identify themes emerging from the interview data, using manual coding techniques to analyse transcripts.

#### **4.4.2 Ethics**

The original randomised controlled trial (CRESSIDA; Cardiovascular Risk REduction Study: Supported by an Integrated Dietary Approach ISRCTN 92382106) received ethical approval from the National Research Ethics Service Committee - Westminster (Ref: 10/H0802/24) in July 2010 and recruitment began in August 2010. The committee approved an amendment for this ancillary study in October 2011, to additionally collect qualitative data using interviews with a sub-sample of participants who had completed the dietary intervention study. Additional signed consent was obtained from each participant who agreed to be interviewed. A small acknowledgement of their

contribution to the research was made through the provision of supermarket gift vouchers to the value of £25.

#### 4.4.3 Participants and recruitment

Participants were aged 40-70 years and were purposively sampled (see below) from the first two cohorts of the CRESSIDA study (n=44). Participants from cohort 1 completed the study between August and December 2010; cohort 2 participants completed the study between January and July 2011.

Participants were recruited from the subgroup of participants randomised to the cardioprotective diet, as this group received a dietary intervention that required them to make self-selected changes to their habitual dietary intake resulting in a dietary pattern that was different to the usual intake of UK adults of similar age. The details of the dietary intervention are provided in Chapter 3 of this thesis. In brief, written and verbal dietary advice, and some foods were provided to aid compliance. Self-monitoring sheets were provided to participants at the follow up visit at week 4 of the protocol, and participants were encouraged to keep track of their food intake against the dietary targets of the study.

To ensure the data collected was theoretically representative of the larger sample of people randomised to the cardioprotective diet group, sampling aimed to capture representation from different age groups, gender, ethnicity and social circumstances (Draper and Swift, 2011), following a process known as 'maximum variation sampling' (Patton, 2002, Sandelowski, 1995) which is a form of purposive sampling. An undergraduate student researcher, who was not involved in other aspects of the CRESSIDA study, approached participants by email or phone to invite them to participate further according to a sampling frame (Table 4.1) in order to remove any potential for coercion from the dietitian researcher, whom the participants were very familiar with as a result of her involvement in the CRESSIDA study.

Table 4.1 Sampling frame used for inviting participants to attend an interview

<b>Intervention completion date</b>	Nov 2010 – Dec 2010			May 2011 – July 2011	
<b>Age (years)</b>	40-49		50-59	60-69	
<b>Gender</b>	Male			Female	
<b>Cohabitation</b>	Partner: yes	Partner: no		Children: yes	Children: no
<b>Ethnicity</b>	White British or White Other		Black / Black African or Black / Black Caribbean	British	Other
<b>Age finished full time education (years)</b>	≤15	16-18	19-25	≥26	Still in FT ed
<b>Employment status during the study</b>	Employed	Not employed	Retired	Other	

Phenomenological studies aimed at understanding people's experiences can yield rich data with around six participants (Morse, 1994) although sample size should be guided by what is

appropriate for the particular research topic based on a number of considerations including ease of obtaining the information on the research question in an interview, breadth of the research topic being investigated and the quality of the data provided by interviewees (Morse, 2000). It has been previously shown that theoretical saturation is possible with between six and twelve participants using interview data (Guest et al., 2006). Eight participants agreed to participate and were interviewed in this study; this number was chosen for pragmatic reasons rather than to achieve data saturation. The decision to stop data collection at eight participants was due to resource limitations, and to ensure adequate depth of analysis could occur with the data generated.

#### 4.4.4 Interviews

Semi-structured interviews were conducted. An interview guide to structure the interviews was developed. In developing a topic list, a deductive approach was taken, using topics generated from the literature and the personal experience of the primary researcher (DR). A list of topics was compiled, from which standard questions were developed to explore the experiences of participants who had completed the study within the previous six to twelve months. A standard introduction and some warm up questions were asked, to help to put the interviewee at ease and open up communication (Draper and Swift, 2011). These were general questions (for example "Remind me about your life/ tell me a little bit about yourself during the study for example where you lived, worked, who you lived with"). Each interviewee was then asked the topic-related questions (Table 4.2), however not necessarily in the same order, as is usual practice in semi-structured interview methods. Some interviewees were asked additional questions in an effort to probe for further details or clarification as they described their experiences.

Table 4.2 Topics explored and standard questions with prompts

Topic guide	Standard questions and prompts relating to topic
<b>Overview of experience of the intervention diet</b>	1.Can you describe for me what you remember about the dietary changes you made whilst following the CRESSIDA diet? <b>Prompts:</b> <ul style="list-style-type: none"> <li>• Change to breakfast/ lunch/ evening meal; change to snacks and drinks.</li> <li>• Different components of the intervention: reduced salt, saturated fat, added sugars; increased fruit &amp; veg, whole grains, oily fish</li> </ul>
<b>Aspects of the diet most/ least enjoyed.</b>	2.What were your overall impressions or memories of following that diet for the three months or so that you were on the study? 3.Were there aspects of the diet that you liked more or less (or were harder/ easier) than others? What were they?
<b>Aspects of the diet easiest/ hardest to implement.</b>	
<b>Aspects of the diet continued beyond the study</b>	4.Have you continued with any of the dietary changes since the study finished? If so, which and to what extent?
<b>Factors or strategies that participants found helped them to follow the dietary advice (Enablers)</b>	5.Were there any factors or strategies that you found particularly helpful or prevented/ limited your ability to make the dietary changes asked of you?

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**Factors or problems that participants encountered that prevented or limited their ability to follow the dietary advice (Barriers)**

**Prompts:**

- Support from family, spouse, friends
- Individual skills such as organising/ planning/ shopping/ cooking skills
- Time available

6. Was the dietary advice provided to you as part of the study more of a help or a hindrance for you in making the dietary changes asked of you?

**Prompts:**

- Verbal advice
- Written information
- Email/ phone support

7. You received reimbursement for fresh oily fish/ some foods you purchased as part of the study.

**Prompts:**

- Did you find this helpful in making the changes?
- Do you think you would have made the changes without the reimbursement of these expenses?

**Usefulness of the food products provided, experience of similar types of food products before/ during/ after the intervention**

8. We provided you with some food products during the study. Tell me to what extent these were a help or a hindrance in making the dietary changes asked of you? Were any more/ less helpful?

**Prompts:**

- Preferences – likes/ dislikes
- Were any of these products totally new to you?
- Have you continued to eat the same/ similar products?
- Approach to supermarket choices before / during/ after the study?

**Physical experiences during the intervention (for example feelings of wellbeing, altered bowel habits, weight gain or loss)**

9. Do you remember experiencing any physical changes whilst following the diet? IF YES: How did this/ these affect your motivation and ability to make and maintain the changes asked of you?

**Prompts:**

- Changes to weight, appetite, bowel habits, feelings of health or ill health
- If has only mentioned only positive or negative changes, prompt for other.

**Emotional experiences during the intervention (for example feelings of control/ lack of control)**

10. Do you remember any emotional things or feelings that occurred during the time you were following the diet? IF YES: What were they and when (which time point) did these occur?

**Prompts:**

- Feeling less/ more in control of daily life/ meals, sense of boredom or excitement surrounding food and meals
- If only mentioned positive or negative, prompt for other.

**Social consequences of following the intervention diet**

11. Did you notice any social consequences (advantages, disadvantages) for you in following the diet? (ie did the diet affect your social life in any way?) IF YES: How did you manage these?

**Prompts:**

- Were you able to go out/ visit friends and family as you normally would?
  - Did you eat meals outside of the home?
-

#### **4.4.5 Data collection**

Interviews were conducted by the dietitian researcher in a quiet meeting room which provided a confidential environment. They took place at the same site as some of the CRESSIDA study visits (Franklin Wilkins Building, King's College London) as participants were familiar with the location. The interviews were recorded electronically for transcription once completed.

Transcription of the interviews was undertaken by an undergraduate student researcher as soon as possible after the interview, and then checked by the dietitian researcher who listened to the audio recording all the way through and checked the transcript for accuracy. Any proposed changes were noted and agreed between the two researchers. A naturalised mode of transcription was adopted, which included as much detail about the transcription as possible, making note of pauses, overlapping speech and laughter as well as the actual text spoken (Oliver et al., 2005).

#### **4.4.6 Data analysis**

A thematic style of analysis was adopted, as described fully in Section 2.7.2 (Qualitative data analysis) in Chapter 2. In brief, a systematic approach was adopted and a constant comparative analysis method was used to code words and sentences from the transcripts into themes and sub-themes. An iterative process, that included independent analysis followed by frequent discussions between two researchers, was used until agreement was reached on the final set of concepts. A conceptual diagram was then generated to represent the themes, sub-themes and their inter-relationships. Following analysis, data was reported as results and discussion to assist with the synthesis of results for the reader.

### **4.5 Findings and discussion**

#### **4.5.1 Sample description**

A total of eight participants were interviewed in this study, including an equal number of males and females (Table 4.3). The majority were aged between 50 and 59 years, employed and had left full time education between the ages of 19 and 25 years. Five participants were living with a partner, and three of those were also living with children in the household. The participant characteristics reflected the purposive sampling framework adopted (Table 4.1).

Table 4.3 Participant characteristics of those interviewed and the whole cardioprotective dietary study sample

Characteristic		Interview sample	CRESSIDA all
		<i>n</i>	<i>N (%)</i>
Gender	Female	4	98 (60)
	Male	4	64 (40)
Age group	40-49 years	1	66 (41)
	50-59 years	5	60 (37)
	60-70 years	1	36 (22)
Employment status	Employed	7	119 (73)
	Retired	1	20 (12)
	Student/ Volunteer/ Home duties	0	12 (7)
	Unemployed	0	10 (6)
Age of leaving full time education	≤15 years	1	9 (6)
	16-18 years	1	65 (40)
	19-25 years	5	66 (41)
	≥26 years	1	17 (11)

#### 4.5.2 Thematic analysis

Dietary change is a complex process, and an understanding of the motivators, barriers and enablers of behaviour change is essential in translating the intervention at a population level. In the analysis of the transcripts, key themes were generated pertaining to the experiences of participants undergoing dietary change as part of a rigorously conducted randomised controlled dietary intervention trial. These themes provide important contextual details that have utility in the wider implementation of the CRESSIDA study, which has demonstrated the efficacy of a dietary pattern consistent with UK dietary guidelines.

Two categories of themes were developed in the analysis of the transcripts – experiential themes and themes relating to strategies adopted during the period of dietary change. There were four experiential themes, and each of these were also arranged into sub-themes to reflect the breadth and depth of concepts brought forward in the interviews (Table 4.4). The themes and sub-themes were often linked and inter-related (Figure 4.1).

Table 4.4 Summary of themes and sub-themes developed from the 1:1 interviews

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**A. Experiential Themes**

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**Theme A1. Participation in a scientific study**

*A1-1 Experience of being a study participant*

- *Scientific rigour and obligation*
- *Finite time period*

*A1-2 Perceived benefits of participation*

- *Financial benefit*
- *Food provision and reimbursement*
- *Information about own health status*
- *Approval of allocated diet*

**Theme A2. Making changes to foods eaten**

*A2-1 Packaged foods*

- *Food label reading*
- *Food provision and reimbursement*

*A2-2 Food preferences*

**Theme A3. Going through a process of habit change**

*A3-1 Perceived similarity of cardioprotective diet with usual diet*

*A3-2 Making and breaking habits; dietary habits retained beyond the study*

*A3-3 Perceptions of difficulty in achieving dietary change*

**Theme A4. Social, physical and mental wellbeing effects**

*A4-1 Wellbeing and physical effects*

- *Feelings of wellbeing and control*
- *Short term physical discomfort attributed to diet*
- *Perceived weight changes*

*A4-2 Social eating (at home with family/ partner and away from home)*

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**B. Strategies adopted in response to dietary experiences**

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**Theme B1. Adopting a prescriptive 'regime'**

*Describing a rigid approach, strict adherence to dietary guidance, developing own checklists and using study guidance material to self-monitor.*

**Theme B2. Personal Skills**

*Personal attributes or skills that the participant had prior to the study or had developed during the study which aided in implementation of the dietary changes.*

**Theme B3. Removal of temptation**

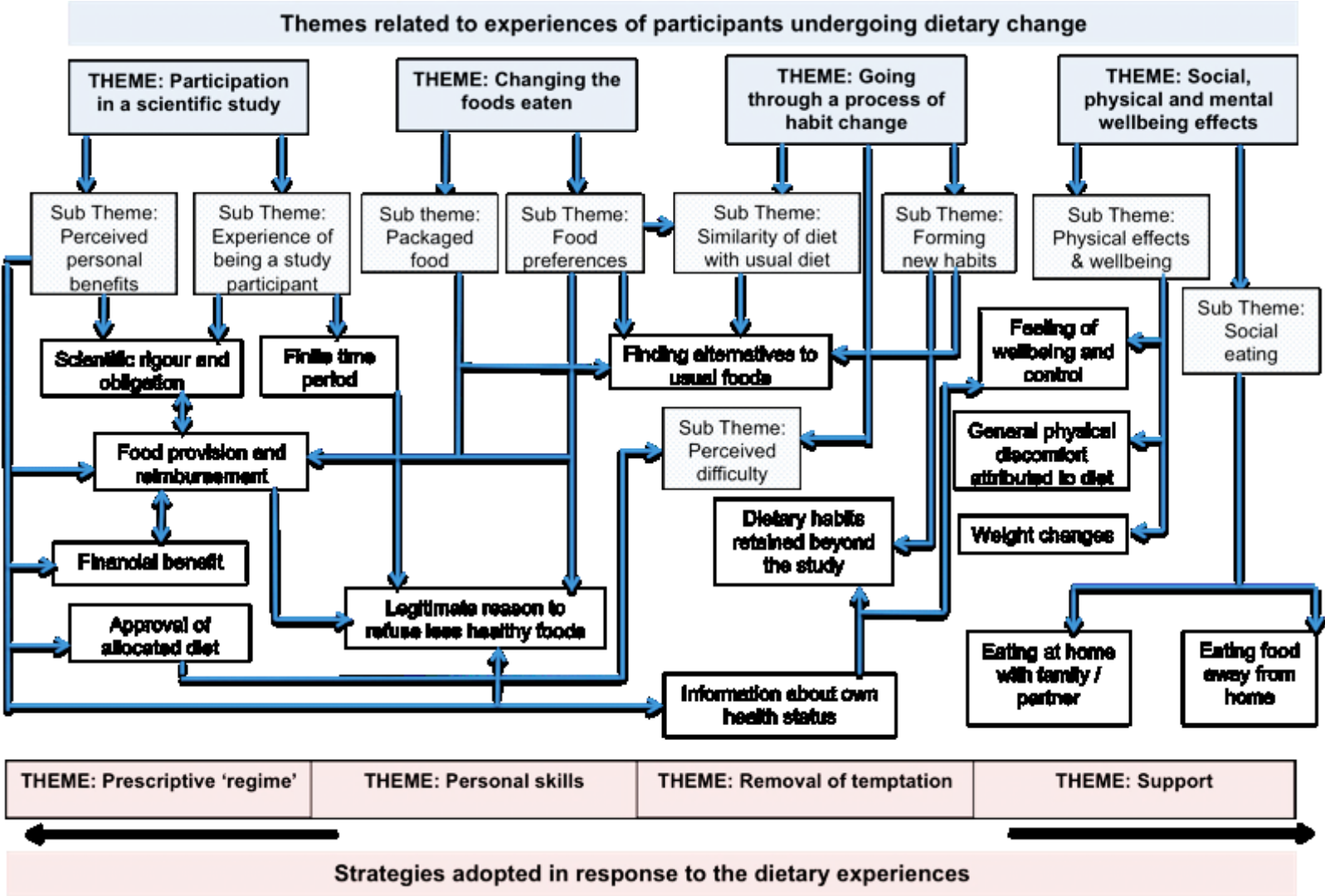
*Describing the removal of temptation as a strategy for following the dietary guidance, either by avoiding the purchase of less healthy foods or by removing them from easily accessible areas.*

**Theme B4. Support – internal and external to the study**

*Social or study-provided support that made the experience of dietary change easier*

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Figure 4.1 Conceptual map of themes developed related to participants' experiences of dietary change and strategies adopted in response





## 4.6 Experiential themes

The first theme related to participation in a scientific study and concepts were organised into two sub-themes (1) the experience of being a study participant which included a personal obligation to scientific rigour and dietary change for a finite period of time, and (2) the perception of personal benefits from participating in the study.

### 4.6.1 Experience of being a participant, obligation to scientific rigour

A strong influence of the experience of being a study participant was identified, which was a clear motivator for dietary change in the participants interviewed. Within this sub-theme, participants described their overall feelings about having participated in the study, individual elements of the study, and interaction with the study team. The strength of this experience was demonstrated by the participants' view that the whole of the study was 'the diet', as opposed to the separate components comprising the dietary intervention and study outcome measures which the researcher had construed in developing the interview guide. Thus when describing their experiences of dietary change, some participants spoke of their experience with the urine collection, BP monitoring and the standard meal the evening before the vascular measures.

*The hardest thing for me was the, was the having the ready meals at the, because that's really alien to us and they're just tiny portions. [Referring to the standardised meals before the baseline and endpoint visits] [Sandra]*

There was a tendency to describe the overall experience as good (positive) or 'harsh' (negative) although the majority of participants reported that they enjoyed the experience overall.

*We really enjoyed being on the study so... it was quite nice [Sandra]*

*Yes my overall impression was it was a very harsh time for me, which if I'd have known it was going to be as harsh, I do remember you warning me but I didn't think it was going to be quite, I was going to find it quite so hard. [Meredith]*

The socio cultural norms of people who volunteer for scientific studies are likely to include a belief in science and the scientific process, and a sense of altruism – that they are contributing to a wider cause. In focus groups conducted with participants from the Oslo diet and anti-smoking trial, a similar theme was developed where participants had a sense of contributing to something that would have benefit beyond themselves as individuals and a desire to be involved in the scientific process (Cable et al., 1999). Numerous other studies have found altruism to be a key motivator for participating in and complying with trial interventions (Emergency Care Research Institute (ECRI), 2002).

Whilst the belief in science may be a unique motivator for the participants in the cardioprotective study, the involvement of more common sociocultural motivators that would increase the success of implementing this dietary change intervention might include celebrities, the mass media and advertising from primary food producers. Celebrity participation in social marketing, messages in the mass media, and advertising have previously been identified as important to public health. Attempts to use celebrities to promote healthier behaviours have had varying success, and have

been used to promote smoking cessation (Chapman and Leask, 2001), HIV prevention (Casais and Proença, 2012), and responsible alcohol consumption (McCabe et al., 2013). Celebrities who publically acknowledge a personal illness, such as breast cancer, colon cancer, Parkinson's Disease have also been shown to increase public awareness of screening and prevention (Chapman and Leask, 2001). In addition, food, nutrition and health are frequently discussed in television news programmes (MacLaren, 1997), popular entertainment programmes (Byrd-Bredbenner, 1998, Byrd-Bredbenner et al., 2001), magazine articles (Guillen and Barr, 1994) and advertisements (Lohmann, 2000) and these prevalent messages are likely to be a strong influence in the wider community (Swinburn and Egger, 2002).

The sub theme also captured the obligation and commitment to scientific rigour and the study. Participants felt obligated to follow the dietary guidance quite strictly, and mentioned specific examples of where they had overridden their own preferences for the sake of 'science'. They expressed the view that they had committed to scientific rigour in volunteering for the study. This was despite dietary advice being designed to fit with different individual preferences and lifestyles, and allowing considerable flexibility to accommodate these. Three participants worked in an academic setting (across administrative, management and research roles) and might have been expected to place a high value on research, however the importance of dietary adherence for scientific rigour applied across each of the interviewees who came from a range of work and educational backgrounds.

*I had no problems making the changes because I just had, I knew I was on the trial and I had to do it. I just carried on doing it... [Barry]*

The qualitative literature exploring compliance factors in dietary (and in fact clinical trials generally) is minimal. A qualitative investigation of participants undergoing dietary change in a weight loss study similarly found participants felt a sense of commitment to being part of a research study and they expressed that they had a sense of responsibility to be more precise with the intervention (completion of self monitoring diaries) as a result (Burke et al., 2009). Following a series of interviews with patients who had consented to participate in clinical trials, an editorial suggested that the significant commitment required of participants may mean that they continue with participation even when they find it overly-demanding (Redig, 2009). Interestingly, a qualitative study of physiotherapy patients suggested initial compliance was influenced by participants' obligation and sense of loyalty to the therapist, but that after three months the effect waned (Campbell et al., 2001) suggesting the compliance effect of such feelings of obligation and altruism may be limited.

The ability to forego their own food preferences for reasons of science and altruism may have been made possible by the knowledge that it was only for a finite time period.

*...actually I stopped on the 20th, I should have stopped on I think it was the 18th but because I had my final appointment, clinical appointment at St Thomas' I had to continue until the 20th, but I took with me to that appointment a packet of really greasy Kettle Crisps chips, which I opened on the way home. [Meredith]*

*It helped cause there was like a finite period of time. [Sandra]*

The CRESSIDA study was not intended to be a 'behaviour change' study, and rather was designed to test the efficacy of a diet consistent with dietary guidelines for improving cardiovascular risk. It is therefore not surprising that some of the participants saw the changes as temporary. Intervention trials of diet and physical activity changes for weight loss rarely report outcomes on maintenance of behaviour change although those published tend to suggest long term compliance is high (Fjeldsoe et al., 2011) which may reflect positive publication bias rather than true maintenance of behaviour change. This same review of randomised controlled trials also concluded that dietary behaviours were more likely to be maintained than physical activity behaviours (Fjeldsoe et al., 2011), although the results of the current study suggest that the changes maintained were not comprehensive with the participants selecting the changes they chose to continue beyond the study (as described in 4.3.3.2 below).

#### **4.6.2 Perceived personal benefits of participation**

Interviewees described a number of benefits that they valued from participating in the study; the strongest of these was the perceived individual benefit they got from participating in the study. Participants described food provision, reimbursement of travel or food items, and the honorarium at the end of the study as a financial benefit that they found motivating.

*I wouldn't have had that much [referring to fruit and vegetables]. That side's a bit limited (**laughs**) and that's the best side, that side should be at the top of my list, that's not my choice. ["That side's" referring to finances] [Josephine]*

Other studies, including those using quantitative methodology, have found similar results. Financial incentives have been found to be effective motivators for changing behaviour in terms of food purchases, food consumption, or weight loss (Wall et al., 2006). The honorarium provided to participants at the end of the CRESSIDA study was small however, particularly given the number of visits and occasions that participants were required to provide 24-hour urine collections and 24-hour BP monitoring, as well as the dietary changes for a 12 week period. Nevertheless, some of the interviewees saw the honorarium as a clear incentive.

Participants also described feeling fortunate to have been randomised to the 'healthier' diet, and described the dietary change as being less difficult as a result of their own approval of the changes required.

*...but I had this sort of feeling that it was actually benefitting me and obviously we're not silly, we sort of realised that we were on the sort of um sort of healthy part of the diet... [Michael]*

The validity of the dietary advice provided, in the eyes of the participants, appears to have been strongly motivating. This fits with the Health Belief Model, which suggests that the perceived effectiveness of a recommended action will influence the adoption or non-compliance with advice to change behaviour (Becker and Maiman, 1980, Chatterjee, 2006). This has important implications for the translation of the dietary intervention to a non-study population who may not have the same confidence in the dietary change advised.

The influence of the mass media on nutrition knowledge and beliefs, previously mentioned, may be an important determinant of the perceptions of the efficacy of advice to follow dietary guidelines. Indeed a study looking at the nutrition messages portrayed in UK newspapers found very few of them to be evidence based (Cooper et al., 2012). In addition, recent opinion pieces in key medical journals, often widely reported in the mass media, have been portrayed as undermining some aspects of current dietary guidance (Malhotra, 2013, Sinatra et al., 2014, DiNicolantonio, 2014). Similar commentary papers promoting the role of simple dietary advice consistent with dietary guidelines (Carlos et al., 2014) receive little or no media attention. Such inconsistency and bias in nutrition messages and the media propensity to highlight controversy over considered evaluation of the evidence base could have a negative effect on the public's confidence in government endorsed dietary advice.

Participants also found the promise of individual feedback about the effect of the dietary change on their own risk factors to be an additional benefit of participating in the study and a strong motivator to comply with the dietary advice.

*...because when I went through the report it said that my cholesterol was something like 6.5 and at the end of it, it was down to 5.5 so I just thought well it's worth... [Gayle]*

Receiving physiological test results was posed as a potential motivator to adopt healthier behaviours to promote cardiovascular risk reduction in a recent systematic review (Garside et al., 2010), based on two studies which reported this - one in the United States of America (Mayer et al., 1998) and one reporting on a family intervention in Merseyside, UK (Peerbhoy et al., 2008). A similar qualitative exploration of the experiences of participants in the Oslo Study Diet and Anti-Smoking Trial also found individual feedback to be an important motivator for behaviour change (Cable et al., 1999).

## **4.7 Experience of changing the foods eaten**

The second experiential theme related to participants' descriptions of their experience of changing the foods they routinely ate. Participants described their experiences of choosing foods to fit with the advice provided to them in the study, and the factors they considered in making those choices. There were two sub-themes developed and these related to (1) experiences associated with packaged foods, including label reading as well as the food provided as part of the study, and (2) individual preferences expressed as likes and dislikes.

### **4.7.1 Packaged food - purchased and provided**

This sub theme was characterised by a general suspicion about the claims on food labels and the food industry generally, the study increasing awareness and understanding of food labels, and confusion about what to buy given the choice of products available in the supermarket. Food provision and reimbursement of select food items was also a major feature of participants' experiences.

*...and you kind of go which is the lesser of the two evils? And definitely if you're going to, if you buy any kind of packaged foods, even though that traffic light thing is kind of useful it's not on everything and it seems to vary on packets and it's so confusing and there's other things. If you don't, if you go in there and you have no idea, you have no idea whether this is good? Whether this is good? I'm kind of a bit suspicious of anything that's um [...] too processed anyway, because something says it's low fat and then you read it and it's got ten tonnes of other rubbish in there you just kind of think what? You know... [Sandra]*

It is possible that these individuals, as study volunteers, were strongly motivated to eat healthy foods but found the range of food marketing terms around health to be confusing and contradictory at times (Garside et al., 2010). The idea that the general public interpret healthy foods as extending to wider concepts of healthfulness (including for example 'organic', 'natural' or home prepared as being inherently better than manufactured food products) than the typical definitions used by nutrition scientists and health professionals has been noted previously (Murcott, 2002). The influence of the internet, mass media and social media in increasing the confusion of consumers may also be a factor (Moritsugu, 2007).

Making use of the food provided as part of the study, along with reimbursement of costs for the purchase of fresh oily fish, was highlighted by all participants. Participants described structuring meals around the foods that were provided, substituting study foods for usual foods, and being willing to try the study foods because they were provided despite being unsure of them.

*I had to plan my meals to fit in. But it wasn't so difficult because the food was given so that helped. I guess if I didn't get the food then it would be harder because I'd have to make sure I buy stuff so it's less stressful having to think about the main details because that was catered for... [Josephine]*

*Well I think the fish because I wasn't a great fish eater before, I think I told you that at the very beginning and I got to like that and it was fine, you know. [Barry]*

Food provision has been shown to be an effective strategy in improving compliance to dietary advice, although surprisingly few qualitative studies have directly investigated this potential motivator. An ancillary study to the 1968 American National Diet-Heart Study showed that providing participants with foods that reflected and reinforced the dietary changes they were being asked to make was more effective in facilitating dietary compliance than providing instructions for purchasing the same foods (National Diet-Heart Study, 1968, as cited by Jeffery et al 1993). Another study which evaluated food provision specifically in improving compliance to weight loss interventions concluded that the strategy was more effective than direct financial incentives in improving compliance (Jeffery et al., 1993).

## 4.7.2 Individual food preferences

Likes and dislikes (food preferences) were also identified as major influences on food choice, with the taste and texture of new foods influencing decisions to include or avoid them. This applied to the foods provided as well as purchasing choices in the supermarket. Individual preferences were also considered when choosing food from restaurant menus, and for some these meals were influenced very much by taste to the extent they were likely to override dietary advice.

*Oatibix which were absolutely terrible and stuck to the roof of my mouth (laughs) and I've put everybody off it since.* [Gayle]

*It still would have been something that I would have had, I still chose something that I would like because otherwise it would be a waste of time going to the restaurant, waste of money, just a total waste and if I go to a restaurant I'm going to choose something I know I will eat.* [Josephine]

That participants talked about their food preferences as key factors influencing their food choice decisions is unsurprising, and likes and dislikes have previously been proposed as a key internal factor driving food choice, independent of external stimuli (Eertmans et al., 2001). The reliance on rational decision making rather than attention to taste, flavour and preference (Rozin and Fallon, 1987) has been a criticism of the use of the Health Belief Model for framing dietary change (Eertmans et al., 2001).

Other qualitative studies have similarly found food preference to be a strong influence on food choice decision-making. A qualitative exploration of food choices of pregnant women with gestational diabetes mellitus also found personal food preferences to have a strong influence (Hui et al., 2014). Another cross-cultural study found that giving up favourite foods was cited as a consistent barrier to dietary change across 15 countries (Lappalainen et al., 1997). However in the current study, there were individuals who had clearly overridden their own food preferences for the sake of the 'study' – Meredith for example describes strategies for incorporating the study foods provided each week using a checklist approach, and then states:

*The things I'm never ever going to eat again, that I disliked were; mackerel, sardines, spaghetti, all pastas, spaghetti, rice and so on, I'm never ever going to eat those again.* [Meredith]

Food preference is influenced by many factors, but cultural identity is known to strongly influence food selection, and has been identified as a potential barrier to healthier eating where the cultural norms value foods that do not fit with the cardioprotective dietary pattern. Although there was limited cultural and ethnic diversity in the sample participating in the current study, similar findings have been documented in other cultural groups (McGee et al., 2008). For example a heart health study in American immigrant Latino populations, dishes with meat as a focus are culturally important and were identified as a barrier to changing dietary habits (Moreno et al., 1997). Similarly a study to change lifestyle factors in Bangladeshi, Indian and Pakistani communities in Edinburgh found cultural resistance to be a barrier to making meaningful changes to cardiovascular risk factors (Netto et al., 2007). It has been suggested that describing cultural or

individual food preferences with the term 'barrier' may invoke negative connotations in the individuals being targeted, prompting rejection or resistance to change. Using wider socio-cultural values with individuals from different social and cultural backgrounds may be more helpful in motivating people to change their dietary habits (Murcott, 2002).

## **4.8 Going through a process of habit change**

The third theme captured participants' descriptions of their experience as a process of change as they reflected on their eating habits before, during and after the study. There were four sub-themes related to (1) perceived similarity of the cardioprotective diet with their usual dietary habits, (2) making and breaking habits, (3) retaining some of the new dietary habits after the study had ended, and (4) perceptions of how difficult (or easy) the dietary change was for them as individuals.

### **4.8.1 Perceived similarity of cardioprotective diet with habitual diet**

The first sub-theme reflected the propensity for participants to relate the requested dietary changes to their usual diet by finding points of similarity as a reference point, although some participants did see the dietary changes as radically different. Participants described the changes as small or large in comparison to their pre-study diet, but were sometimes contradictory during the interview. They also spoke of foods they usually ate as being similar or different to the foods provided as part of the study, and the process of finding suitable replacements for foods they had enjoyed previously.

*I'm contradicting myself a bit here ... because it was quite easy to follow ... because it wasn't too dissimilar to our own diet we have anyway. [Michael]*

*So there were changes, major changes I think to my diet in that period so every day almost every meal was different probably to what I would normally have had. [Peter]*

*...yes you gave me the muesli yes I quite liked that. Yes I mean if I had to have something other than my bacon that would have been a nice option but I haven't kept on with it, I'm back to my bacon and my toast... [Meredith]*

The fact that participants in the current study recognised (or failed to recognise) aspects of their own dietary habits in the dietary advice provided may have been a strong facilitator (or barrier) for them making the required changes. The perception that the dietary change is too different from the individual's current diet has been previously reported as a barrier to healthier eating (Lappalainen et al., 1997). However, the perception of dietary habits as similar to the advice provided does not necessarily mean that actual habits reflect this perception. Several studies have noted participants' own perceptions that they comply with complex dietary advice such as fruit and vegetable consumption and lower fat intakes (Lechner et al 1998) whilst their actual behaviour does not actually reflect such behaviour (Bogers et al., 2004, Lechner et al., 1998).

## 4.8.2 Making or breaking habits, retaining new habits beyond the study

The second sub-theme drew out the experiences of participants in making or breaking habits, particularly in the initial stages after receiving the dietary advice as part of the study. Participants spoke of the change as a process they went through, describing the breaking of old dietary habits, and the forming of new habits that were more aligned with the dietary advice. Elements of their food preferences were also included in these discussions, as they were what their usual habits were based on. Some of the new habits were retained beyond the study, and these were described. Most of those habits retained were those that were perceived to be enjoyable, whereas those that were more of a chore during the study period were not persisted with.

*I just kind of looked at that and I looked at what was required and I just kind of included it in my normal day. I mean I did take a little while to get used to it but it just became natural after a while ...* [Josephine]

*Then when the diet finished, slowly but surely I got back into my old ways but I didn't rush it you know, for a few days after I didn't really bother because I hadn't missed it for 3 months and that, that's the only change to my life really.* [Barry]

Eating behaviour has been described as a largely habit-driven activity (van't Riet et al., 2011). A study looking at behaviour (including eating and drinking) and habit formation in the real world demonstrated large individual variation in the number of repetitions required for an activity to become a habit, ranging from 18 to 254 days (Lally et al., 2010) but there has not been much research into the experience of breaking old dietary habits and replacing them with new habits.

In the present study, creating new habits (and breaking old habits) was seen as particularly difficult in the initial stages of dietary change. The first two to three weeks was identified as most difficult by one participant, whilst others didn't put a time frame on the most difficult period but identified it as being in the initial stages. Participants described the change as re-establishing a routine around different foods and not being able to automatically select and prepare foods that were suitable. As part of this process, participants seemed to identify those aspects of the intervention diet where they perceived they were close to or already eating foods that were consistent with the new pattern of eating, along with aspects where they needed to make major changes. They then described how they went about finding replacements for foods that were previously part of their day-to-day repertoire of foods eaten. These were seen as new habits that replaced the pre-study routine and extended to supermarket as well as restaurant food choices.

## 4.8.3 Perceptions of difficulty in achieving the dietary changes

There were differing perceptions evident between participants about how difficult the process of dietary change was for them during the study. The male participants tended to be more likely to describe the changes as easy to make, whereas although some female participants also claimed



the changes were easy to make this was not consistent and they were less emphatic in their responses.

*Well because I was eating healthy food, fish and fruit and.. I don't see how that can be hard for anyone. [Allan]*

*Fruit and vegetables is always the hardest part. The rest was easy to follow. [Josephine]*

A qualitative study that conducted focus groups with people aged 25-70 years in small rural communities in the United States of America found that about half of the women and older men found previous dietary change relatively easy, the other half had found it difficult. Younger men (aged less than 45 years) with children at home almost unanimously reported finding dietary change very difficult (Iszler et al., 1995) – as our sample was drawn from men who were older than 45 years it is possible that this reflects their stage of life and living situation, which may make dietary change an easier proposition.

## **4.9 Social, physical and mental wellbeing effects**

The final experiential theme encompassed the participants' descriptions of their perception of following the cardioprotective diet and the effects on their physical, mental and social wellbeing which each of the interviewees described and seemed to attribute to the dietary changes they had made. These experiences were categorised into five sub-themes which were (1) a sense of wellbeing and feeling 'in control', short term physical discomfort related to the diet, and perceived weight changes, and (2) the social effect of the diet when they ate away from home or when they were with family or friends in their own or others' homes,

### **4.9.1 Wellbeing and physical effects**

Participants described feelings of wellbeing and health, as well as feeling more control over their eating whilst following the dietary advice provided. Individuals varied in how they expressed this, with some acknowledging the effect was possibly 'psychological' [Peter] or a 'placebo' [Sandra].

*I probably had more control over, although you were giving us the diet, you still felt that because as it was planned out like I said before there was more control maybe and also there was this underlying element that I felt it was going to be doing good so that was kind of an incentive in a way. [Michael]*

*I felt quite good, I felt quite good all round. [Josephine]*

Four participants reported physical discomfort which they attributed to the different foods they were eating as part of the intervention dietary pattern. They described various negative symptoms including wind and gastrointestinal pain, hunger, fatigue and a positive from one participant in the apparent improvement in premenstrual symptoms whilst following the diet.

*I think, I've got no evidence for it, I think I was more tired to start with. I think my salt content was probably going down quite a lot. I think at the beginning of the diet my blood pressure was probably on the lower side anyway so I felt a bit*

*drained at times and because I do a lot of running I was occasionally you know, I'd have to have something a bit saltier. [Peter]*

The negative symptoms were described as short term, occurring in the initial stages of dietary change, which resolved spontaneously. Despite experiencing these negative symptoms, participants also described increased overall wellbeing whilst following the diet. The possibility that these feelings may have been due to psychological or a 'placebo effect' was acknowledged by three of the participants.

Hunger has been documented as a negative aspect of healthier eating (Lappalainen et al., 1997). In addition, it is well known that increases in dietary fibre are associated with gastrointestinal side effects such as increased flatulence, abdominal cramping, bloating and changes in the frequency and consistency of bowel movements (Davidson and Maki, 1999, Aro et al., 1981, Ray et al., 1983, Swain et al., 1990).

Many of the participants spoke about body weight changes. All the males who reported they lost weight during the study also claimed they were not aware of the loss until their weight was measured at the endpoint visit. The female participants by contrast seemed to have been very aware of the changes in weight they may have experienced all the way through the study.

*I was hoping I'd lose some weight (laughing) but you said it wasn't for losing weight and I didn't, I thought damn, that was my only disappointment. (laugh) [Josephine]*

*I don't think I felt any different except because I was aware of the weight loss I sort of thought I'm, I'm undernourished. [Meredith]*

*When I came for one of the measurements I thought I was fatter round the waist because I had those nut bars and I think we thought I was eating too many, they were very nice. (laugh) [Gayle]*

The average change in weight over the 12-week dietary intervention for the individuals selected for the current study was -2.6 kg, which is greater than the mean change in the intervention group as a whole (-1.3kg). It is possible that the group that was interviewed were therefore more aware of their weight change than others randomised to this group. However a study looking at gender differences in food choice found women tended to have greater weight control involvement (tendency to adopt 'dieting' habits) and stronger beliefs in healthy eating (Wardle et al., 2004) and these may be potential reasons for the different experiences of men and women in this current study.

#### **4.9.2 Social eating**

Participants described their experiences of eating away from home during the study with the majority finding the dietary advice constrained their choice and at times made them feel uncomfortable in a social situation. Finding situations involving eating away from home as being more troublesome than food prepared in their own home environments has been previously reported as a barrier to dietary change across different populations and environments (McGee et al., 2008, Iszler et al., 1995, Lloyd et al., 1995, Lappalainen et al., 1997). Interviewees in this

study also described how they dealt with the difficulties they perceived – some reacted by telling people in detail what the restrictions were, whilst others preferred not to disclose the fact they were eating differently. Participants talked about how they reduced the frequency of eating socially during the study, a strategy that was also reported in a study which interviewed women with gestational diabetes (Hui et al., 2014).

*Yeah she was ok, if she wanted to go out she would go out with her daughter and I'd stay in so it didn't make any difference you see really. [Talking about the effect on his wife of not going out to eat during the study] [Barry]*

Others in this study accepted that they would not be able to follow the dietary guidance perfectly in social situations but didn't reduce the number of occasions that they ate out. A number of participants acknowledged the difficulty in eating with family (in their family's homes) as particularly difficult because it created tension for the participants themselves but they also perceived it created stress for family members providing food and not as familiar with the dietary guidance. Eating foods that were different to what they would normally have with friends and family was seen as difficult by many of the participants, although three also described that eating out had not been an issue at all.

There were also descriptions of support (or lack of support) from partners, family and friends.

*And very kindly when I went to my nephews for Easter when I was there I think 5 days, very kindly my niece in law as it were, had, I'd told her about it before I went and she had got me the brown bread, the wholemeal bread and she'd also and I took my muesli with me, that was right. [Meredith]*

*Well over the 3 months they just didn't, everytime we went round, 'oh you still on that diet,' 'yeah afraid so.' (laughter) so it was just, you know, it was it wasn't really an issue but I suppose it could have been if you'd have had a bit of a cake or and then I suppose even one bit of cake isn't going to be too harmful as long as you're not taking the whole cake home. [in response to interviewer question as to whether his family kept offering biscuits and cakes over the whole of the study] [Michael]*

The experience of people offering them food that did not fit the dietary guidance was described by half of the interviewees. Two of the participants, both female, also described a positive experience whereby they felt the study legitimised their refusal of less healthy food in a social environment where typically they felt pressured to eat outside of the dietary guidance, particularly in the workplace.

*It sort of gives you the chance to not eat things that you really don't want to eat (laughter) [Josephine]*

## 4.10 Themes based on enablers identified by participants during the study

Interviewees described particular strategies that they adopted during the study to help them make the dietary changes whilst still maintaining their usual day-to-day activities. These were developed into themes which were (1) the adoption of a prescriptive approach, (2) removing sources of temptation to avoid certain foods, (3) applying personal skills such as organisation, shopping, cooking skills, and (4) seeking support, either internal or external to the study.

### 4.10.1 Adopting a regimented or prescriptive approach

The first theme described a prescriptive approach adopted by participants that seemed much more rigid than intended. The participants used terms like 'regimen' and 'legalistic' to describe their approach each day.

*No no, I wanted didn't want them, no. It's like you know that, it's like giving up smoking or something it's the road to ruin. One salted nut, that will lead to a packet. (laughter) [Michael]*

Some took this prescriptive approach further, developing and using self monitoring checklists. These were based on study resources (written dietary material and the study food quantities). Although participants were provided with a self monitoring tool as part of the first follow up dietary visit (week 4 of the protocol), they were asked to only complete this for a week if they felt it would be helpful. Some of the participants interviewed seemed to have taken the checklist approach further by incorporating into their checklists the amount of different food items that had been provided as part of the study had to be eaten in the quantities provided over that time period.

*...and I made a list of the things that you wanted me to have and I ticked them off each week. I had this diary in which I recorded what I had and I had this checklist of what I'd got to have either the mackerel, tin of mackerel or the tin of sardines a week and I had to have pasta once a week and whatever the other, well I knew I was having brown bread and so on, so it was just a matter of following the list. [Meredith]*

All of the participants described following the dietary guidance quite strictly, and seemed to use it as a prescription, describing it as a 'regime' and 'legalistic'. Clear goals have previously been shown to increase the likelihood of dietary change, and individuals who target specific behaviours have been noted to do better than those with comparatively less targeted goals (Calfas et al., 2002, Cullen et al., 2001).

Most of those interviewed in this current study indicated that they liked the extensive written guidance provided as part of the intervention, as they used it as a reference to guide food choices. Taking a prescriptive approach seemed to make it easier for them to comply, which is contrary to other studies that suggest culturally tailored programmes that involve participants in goal setting and developing the intervention are more effective (Moreno et al., 1997, Netto et al., 2007, McGee et al., 2008, Hui et al., 2014). Similar dietary intervention programmes delivered to

free living individuals have also found goals that are assigned by a health care professional to be very effective (Appel et al., 2003, Diabetes Prevention Program Research Group, 2002). It has previously been reported that 'experts changing their minds' is a significant barrier to dietary change for some people (Lappalainen et al., 1997) so the clear guidance may have been appealing for this reason.

The strong influence of being a part of a study would also be very likely to interact with this theme, as the need for 'scientific rigour' would support a prescriptive dietary approach. This was one of the findings of a study looking at the efficacy of self-monitoring as part of a weight loss intervention where participants highlighted 'preciseness' to be important and linked to their sense of obligation to the study (Burke et al., 2009).

#### **4.10.2 Personal skills**

This theme categorised the personal attributes or skills that the participant had going into the study or had developed during the study which they brought up as helpful in making the dietary changes. These included shopping, label reading, cooking, planning (sometimes using the checklists developed as described in 5.1.3.1 above) and organisation skills (including working in partnership with other members of the household). Some of the skills were brought up in the context of a lifetime of gaining them, whilst others such as label reading were acknowledged to have been developed as a result of their experiences on the study.

*I know it sounds... God this guy's not very free, but we'd actually plan the week so it actually made sense so we knew what we had provision wise and what was provided and what we needed to get and that stuff so in that respect it was good. [Michael]*

*I do the breakfast in a morning, that's my job, I've always, I've always done that. She does the evening meal. [Referring to his wife, how they organised the meal preparation]. [Barry]*

Self-monitoring techniques have been demonstrated to increase success in achieving behaviour change (Cullen et al., 2001) and have been suggested as a predictor of maintaining changes longer term (Artinian et al., 2010). Similarly food preparation skills (Lappalainen et al., 1997, Iszler et al., 1995), and difficulties in interpreting food labels in particular (Hui et al., 2014) have been previously highlighted as major barriers to dietary change. Other qualitative reports of intervention studies have also identified that food product label reading education was identified by participants as a key skill and knowledge area, in order to comply with the dietary advice provided (Burke et al., 2009, Hui et al., 2014)

#### **4.10.3 Modifying the environment: removal of temptation**

Female participants described removing food items to avoid temptation as a strategy for following the dietary guidelines, either by avoiding the purchase of less healthy foods or by removing them from easily accessible areas. One participant discussed how she used a shopping list to avoid temptation and keep to her weekly plan for meals. Other individuals spoke of removing foods that

were not aligned with the study guidelines and either giving them away or hiding them in a location that wasn't easily accessible.

*I put them all upstairs because I had some chocolates left over from Christmas which people had given me and I went and gave a lecture to a women's group in the evening and they gave me a lovely big box of roses chocolates, they all went upstairs in my spare bedroom. [Meredith]*

This strategy was described across both the home and work environments, and has previously been proposed as one intervention for breaking established dietary habits (van't Riet et al., 2011).

#### **4.10.4 Support external and internal to study**

This theme captured the participants' responses to questions around social or study resources that influenced their experience of dietary change in some way. Support, whether formally provided as part of the study or in the form of people external to the study, were also seen as helpful in making the dietary changes.

External support (or lack of support) described included family members (parents, children, partners, colleagues and friends).

*Especially with evening meal yes, because the evening meal changed. Breakfast or lunch had no difference at all because I got used to that but it made an effect on the evening meal because she did the fish, the rice and that and I got to like that. [Referring to importance of his wife's support in making changes to the evening meal] [Barry]*

Some participants described family as being supportive, whilst others thought they could have been much more helpful. Two participants elected not to disclose to others that they were changing their dietary habits. Support and encouragement from family and friends has previously been reported as a strong motivator for some people undergoing dietary change (McGee et al., 2008, Netto et al., 2007) but has also been represented as a potential barrier (Fukuoka et al., 2014, Lloyd et al., 1995).

*I didn't feel I needed anybody's support with this, not friends or family, I mean my daughter knew I was doing it, that was it. [Josephine]*

Different participants valued different aspects of the formal support provided through the study (internal support) such as the written material provided and the contact with the study team including the dietitian. The provision of food products was consistently seen as very helpful. This may have removed a potential barrier which has been previously described, in that people are reluctant to spend money on new foods which are seen as a potential for waste if they are not enjoyable (Garside et al., 2010). However other support provided as part of the study was viewed inconsistently between the participants. One older female participant found the written guidance to be complicated, whilst others seemed to value the comprehensiveness of material given and even shared it with family members so they were able to understand the changes they were being asked to make.

*It was quite comprehensive, I mean you got that green folder which was really useful and having the sort of, the food parcels influenced what I had [Peter]*

*No I don't think they, I mean it's good to keep in touch always but I don't think they influenced my behaviour. [Talking about the follow up visit, phone call and email support] [Meredith]*

#### **4.11 Application to community and population based strategies for dietary change**

A number of motivators were sociocultural, including altruism, a belief in science and the experience of participating in a scientific study. Whilst these may not be directly transferable to the wider community, involvement of more common sociocultural motivators that would increase the success of implementing this dietary change intervention might include celebrities, the mass media and advertising from primary food producers.

Individual elements of the experience were highlighted that could be implemented and transferred outside of a scientific study environment. Many of these have been previously reported in the literature. The provision of pantry items consistent with the dietary guidance enabled participants to implement the changes quickly and with less anxiety about food choices and identifying replacement foods for those they usually enjoyed. The initial period of change was thus able to be structured according to the core foods provided. The provision of foods was also seen as a financial benefit, and was an additional motivator for some. Where hospitals provide nutritional supplements at a considerable health budget cost, community based provision of staple foods such as tinned oily fish, spreads, portion controlled raw nuts, wholegrain rice, pasta and breakfast cereals for a short period may be a worthwhile investment to promote dietary change.

In addition, receiving regular feedback on their dietary choices coupled with support and guidance to encourage further changes is easily replicated in the current health system. Monitoring for undesirable side effects of dietary change, such as gastrointestinal discomfort, would proactively ensure the intervention could be individualised to minimise problems. Social support is often already considered in the implementation of interventions, and could be tackled through a combination of population wide promotion and the encouragement of joint dietary change with family and friends. Development of personal skills in shopping, food preparation and meal planning are also features of existing services that could be integrated in a coordinated implementation plan. Building small successes in skill development may also have an added benefit in improving overall self efficacy (Bandura, 1998).

#### **4.12 Strengths, limitations and reflexivity**

The sample size was small and selected pragmatically due to limited resources, so theoretical saturation is unlikely to have been achieved. However there is evidence that this occurs more often in qualitative research than authors admit to – a study of PhD theses using qualitative interviews found the most common sample sizes to be whole numbers suggesting pre-determined sample sizes rather than true saturation. It may be even more so in mixed methods research,

where resources are stretched between both quantitative and qualitative study designs (Teddle and Yu, 2007).

This study was an exploration of the experiences of people who had volunteered to participate in a randomised controlled dietary intervention trial, using a predominantly quantitative approach. The concept and protocol for the qualitative study was developed after recruitment to the quantitative study, and the interviews were conducted during recruitment for the third of four cohorts for the CRESSIDA study. This limited the number of participants that could be interviewed, as resources, particularly time, were taken up by the quantitative study. In addition the design of the study was opportunistic rather than a planned, more generalizable qualitative approach whereby a well-developed theoretical framework is used to draw a diverse sample to derive an explanatory model that applies to a broad range of settings (Gibbs et al., 2007).

Given that the interviewer was the dietitian who delivered the dietary advice to participants, it is possible that interviewees might perhaps have reservations about being honest and comprehensive in their responses. The possibility of a power differential between the interviewer and the interviewees might also have affected open communication. However, all efforts were made to put participants at ease and to investigate views on both the negative as well as the positive experiences in questioning and further probing. However, the position of the dietitian interviewer also brought its own perspective to the interview and has advantages (including an in depth understanding of both the intervention and the participant's lifestyle) as well as disadvantages, and does not make the findings less valid (Hammersley, 1993). In addition, the interpretation of the data was based on one dietitian's perspective (with triangulation from a student dietitian researcher), however another perspective may yield different themes and interpretations.

One of the main strengths of this study was the additional data it adds to the randomised controlled trial, as a result of the qualitative nature of its design which sought to allow participants to provide their own views and opinions on the experience of undergoing dietary change as part of a randomised controlled dietary intervention study. Qualitative methods provide rich and diverse data that is not possible through quantitative means (Cable et al., 1999) and the results contribute to an analysis of the clinical transferability of the study. The results provide valuable translational information, allowing insights into the experiences of participants in a rigorous quantitative study which is rarely reported. In the future quantitative research studies investigating the efficacy of dietary interventions should consider the inclusion of a qualitative component that draws out the experiences of participants, to better inform the transfer to non-trial environments.

#### **4.13 Conclusion**

The themes generated may be best used to develop a more comprehensive and methodologically sound qualitative investigation of dietary change (Gibbs et al., 2007). The barriers and facilitators to change described by the interviewees are applicable to both researchers and dietitians in practice who may be interested in maximising compliance to dietary patterns, and the strategies adopted by participants during the intervention should inform the design of future interventions.



## **Chapter 5 The cost of a cardioprotective diet**

### **5.1 Introduction**

Despite overall improvements in the health of the United Kingdom (UK) population, health inequalities - represented by an uneven distribution of morbidity and mortality - have widened (Department of Health and Public Health England, 2014). The burden of chronic illnesses including CVD is known to disproportionately affect populations of lower income (Bambra et al., 2009a). It is estimated that around a half of the variation in CVD morbidity and mortality between the least and most deprived populations is explained by modifiable risk factors such as smoking, high alcohol consumption obesity, physical inactivity and poor diet (Scarborough et al., 2011).

Social factors such as the cost of food and drink are recognised as important contributors to chronic disease risk development (Butland et al., 2007) however it is difficult to accurately define the relationship between food choice and price. Elasticity of demand is an economic concept concerned with the change in purchasing habits of consumers in response to the change in price of a commodity (Okrent and Alston, 2011). Multiple factors affect elasticity including those at the individual level such as income, age and the number of people making up a household, as well as the price of non-food items like housing and fuel (Butland et al., 2007). A recent systematic review into the effect of price elasticity on demand concluded that higher elasticity (and therefore a greater potential for price to have an impact on population purchases) was evident for some foods more than others including food consumed away from home, soft drinks, juice, meats, and fruit (Andreyeva et al., 2010). During periods of economic instability, the effect of price elasticity on food purchasing is less certain. Over a six year period, median incomes in the UK have fallen by around 8% (Office for National Statistics, 2013d) whilst food price inflation has been estimated at around 17.5% (Department for Environment Food & Rural Affairs, 2013), higher than general inflation (12.8%) (Office for National Statistics, 2013b).

In a recent survey, food prices were identified as an area of concern for more than 60% of UK consumers (Food Standards Agency, 2014). In response, consumers appear to be buying less food, and purchasing cheaper products within the same food category ('trading down' and spending less on food overall). Some researchers contend that there has been a decline in the nutritional quality of food purchased with a trend for processed sweet and savoury foods to be substituted for fruit and vegetables (Griffith et al., 2013). The overall amount spent on household food has declined with a reduction in both food energy purchased combined with a reduction in real price paid per unit of food energy, suggesting a mass of substitution for cheaper products.

### **5.2 Effect of income on diet selection**

The majority of UK adults do not meet government dietary guideline recommendations (Bates, 2012) with more marked areas of concern noted in low income groups compared to the general population (Nelson et al., 2007a). Proportionately, those on lower income spend more of their budget on food than those of higher incomes, estimated at 16% versus 11% respectively (Office for National Statistics, 2013b) and are more greatly impacted by increases in food costs.

Furthermore many strategies employed by higher income households to reduce food costs are less effective for those on lower incomes: for example 'trading down' to cheaper products is unlikely to help those on lower incomes, as they are often already purchasing the cheapest options. In lower income groups, spending on recreation, health and transport is often reduced to offset the increase in proportion of income spent on food (Department for Environment Food & Rural Affairs, 2013).

In terms of dietary quality, people on lower incomes consume similar nutrient profiles but their food choices differ to those on higher incomes. The UK Low Income Diet and Nutrition Survey (LIDNS) noted higher intakes of NMES in low-income groups (Nelson et al., 2007b), more fat spreads, whole milk, table sugar, sugar sweetened beverages, meat and processed meats, and less wholemeal bread, fruit and vegetables than the general population (Department for Environment Food & Rural Affairs, 2013, Nelson et al., 2007c). These findings have been supported in the recent Health Survey for England which found that people on higher incomes were significantly more likely to consume five or more portions of fruit and vegetables per day compared to people of lower income (Joint Health Surveys Unit et al., 2012).

Direct food costs are not the only factors determining affordability of food for low-income households. Indirect costs, such as time, transport, cooking facilities and skills are crucial and are resources that may also be limited (Caraher et al., 1998). Time in particular is a resource often cited as a reason for poorer eating habits, and indeed poverty can be defined in terms of limitations in both physical resources and time (Heggeness et al., 2012). Food purchase and preparation are time consuming activities that can be made less so through 'buying' help – for example through the purchase of pre-cut meats, prepared fruits and vegetables, ready prepared and restaurant meals. Those on higher incomes may also compensate by buying in services such as childcare or help with domestic tasks (Jabs and Devine, 2006), whilst individuals and families on low incomes are less able to compensate for time poverty in this way. In addition a lack of accessible and convenient transport may mean that access to healthy and affordable food is more challenging (Preston and Rajé, 2007) or more time consuming (Jabs and Devine, 2006).

### **5.3 Cost of healthy eating**

A number of cross-sectional studies across a number of countries have modelled the cost of healthier dietary patterns and consistently found them to be more expensive than less health promoting diets (Townsend et al., 2009, Aggarwal et al., 2011, Bernstein et al., 2010, Andrieu et al., 2006, Schröder et al., 2006, Lopez et al., 2009). Specifically in the UK, the Women's Cohort Study found that the amount of money spent was predictive of healthier eating (Carter and Little, 2007) and healthier dietary patterns were found to cost twice as much as less healthy dietary patterns (Morris et al., 2014). Further, the UK NDNS found energy intake to be strongly correlated with dietary cost, and lower food costs for some sub-groups of the population including people in low-income categories and those who consumed less than recommended quantities of fruit and vegetables (Timmins et al., 2013a). Pooling data from the published studies, a meta-analysis was recently published which concluded healthier foods and dietary patterns are more expensive than less healthy foods and patterns (Rao et al., 2013).

Despite this consistent finding across multiple studies and countries, intervention studies that cost changes in actual food intake do not consistently show higher costs associated with higher quality diets. A number of studies, including the Finnish Diabetes Prevention Study (Ottelin et al., 2007) have shown no change in costs (Cleary et al., 2012, Goulet et al., 2008), whilst some have shown decreased (Burney and Haughton, 2002) or increased spending (Rydén et al., 2008). Despite this literature, no costing of UK intervention studies has been published to date. There is a need to assess the financial impact of changing habitual food intake to reflect a healthier dietary pattern in a UK context.

## **5.4 Hypothesis**

Changing to a cardioprotective dietary pattern (cardioprotective diet) will be more expensive than a dietary pattern representative of many adults in the UK (conventional UK diet).

## **5.5 Study aim**

This study aimed to determine if a cardioprotective dietary intervention based on UK dietary guidelines was more expensive than a conventional UK diet.

## **5.6 Methods**

This study consisted of a retrospective analysis of food records completed by participants who were recruited for and completed the CRESSIDA study, a twelve-week dietary intervention study. A description of the original study methods and results has been reported in detail in Chapter 3. Briefly, 162 healthy participants aged 40 to 70 years were randomised to either a cardioprotective diet (n=80; based on current UK dietary guidelines (National Institute for Health and Care Excellence, 2006, National Institute for Health and Clinical Excellence, 2010): salt restricted to less than 6 g per day, SFAs less than 10 % energy, increased whole grains to greater than 50% cereal intake, five portions fruit and vegetables per day and increased fish intake to two portions per week, one of which should be oily) or a control diet (n=82) which was a dietary pattern representative of one eaten by many people in this age group in the UK (Bates, 2012).

### **5.6.1 Participants**

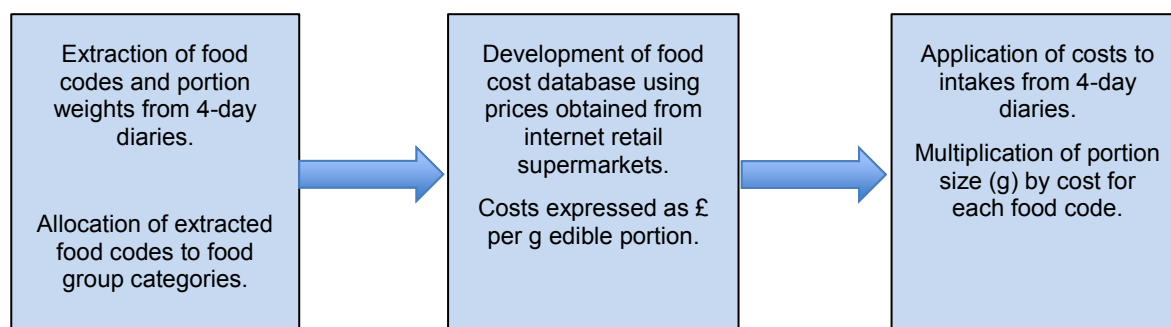
For this study, a feasible sample of 40 CRESSIDA participants (n=20 randomised to the cardioprotective diet, n=20 randomised to the control diet) were randomly selected using a computerised random number generator. An equal number of male and female participants, and those allocated to the intervention and control groups, were included in the sample.

### **5.6.2 Food cost data**

Detailed methods for the food cost data collected are provided in Chapter 2 under Section (Dietary costing methods); and summarised in Figure 5.1. Briefly, each participant completed a food diary at baseline and after 12 weeks on either the cardioprotective or control diet. A list of foods and portion weights was generated from the diaries. A food cost database was developed

using prices obtained from a range of internet retail supermarkets. For each participant at each time point, edible portion food costs were calculated by multiplying the weight of each food item by the unit cost in pounds sterling. Total costs of all food and beverages consumed over the four days were then averaged to derive a mean daily cost. Foods were categorised into one of twelve food groups to assess changes in the weight and cost of each food group during the intervention.

Figure 5.1 Overview of methods used to assign costs to foods recorded in 4-day dietary diaries at baseline and 12 weeks later



### 5.6.3 Data analysis

All statistical analyses were performed using SPSS Statistics software (Version 20.0: IBM Corp, Armonk NY). Distributional checks for normality were undertaken using P-P plots. Paired t-tests were used to compare mean baseline and endpoint costs within each group. Independent sample t-tests were calculated to assess differences between groups for mean change in costs from baseline to endpoint between groups, mean change in weight and daily cost by food group, and mean cost at endpoint by food group.

The difference in amount of food and costs according to food group categories between the groups at endpoint was analysed using ANCOVA, with baseline cost as a covariate.

## 5.7 Results

### 5.7.1 Baseline characteristics

Intakes for 40 CRESSIDA participants' (cardioprotective n=20, control n=20) four-day estimated food diaries were costed at baseline and endpoint (12 weeks later). There were no differences between baseline characteristics for the costed sample compared to all participants completing the CRESSIDA study (Table 5.1), apart from sodium intakes which were higher in the costed sample.

Table 5.1 Baseline characteristics of participants in the costed sample, and all participants who completed the cardioprotective dietary intervention study

Characteristic	Costed Sample <i>n</i> =40	All CRESSIDA <i>n</i> =162	<i>P</i> value*
Age years	52.0 ± 8.5	52.6 ± 8.0	0.68
Gender M/F	20/20	65/99	
BMI kg/m <sup>2</sup>	25.1 ± 3.6	26.1 ± 3.9	0.14
SBP mmHg	118.4 ± 16.3	119.9 ± 16.0	0.58
DBP mmHg	76.9 ± 7.9	78.7 ± 9.6	0.27
Energy – kcal/d**	2327.5 ± 647.3	2130.4 ± 564.6	0.06
Protein g/1000kcal	40.7 ± 8.1	39.8 ± 7.6	0.51
Carbohydrate g/1000kcal	119.7 ± 17.1	119.7 ± 18.8	0.99
Fat g/1000kcal	39.8 ± 7.7	39.3 ± 6.8	0.71
Saturated fat g/1000kcal	13.3 ± 4.1	13.2 ± 3.7	0.94
Fibre g/1000kcal	10.8 ± 3.6	11.4 ± 3.7	0.35
Sodium mg/1000kcal	1704.2 ± 481.9	1493.4 ± 395.9	<b>0.004</b>
(Salt*** g/1000kcal)	(4.3 ± 1.2)	(3.8 ± 1.0)	
Sugar g/1000kcal	51.3 ± 16.4	51.8 ± 14.6	0.83

Values are mean ± standard deviation. M=male, F=female, BMI=body mass index, SBP= systolic blood pressure, DBP=diastolic blood pressure, kcal=kilocalorie \**P*-values are from independent samples t-test. \*\*Energy between groups is approaching significance, likely due to the higher proportion of males in the costed sample (50%) compared with the overall CRESSIDA sample (around 33% male). Therefore the rest of the nutrient data is presented as g (or mg) per 1000kcal \*\*\*Salt values calculated by multiplying sodium values by 2.54 then dividing by 1000.

### 5.7.2 Change in diet cost during intervention

At baseline, diet costs were similar between the cardioprotective and control groups; the mean daily food cost for all participants was £6.12 ± 1.83 per day (data not shown), ranging from £5.22 ± 1.57 in the budget supermarket to £7.78 ± 2.43 in the quality supermarket (Table 5.2). There were no significant differences between groups for any supermarket.

There was no significant change in diet costs between the groups at endpoint for any supermarket. The mean difference in cost at endpoint ranged from -£0.33 (regular supermarket) to £0.09 (budget supermarket) for the cardioprotective dietary group compared to the control group, but these differences were not significant for any supermarket (Table 5.2).

Table 5.2 Daily cost and mean difference in cost of diet for cardioprotective and control group by supermarket

Supermarket	Cardioprotective (n=20)		Control (n=20)		Mean difference £/day (95% CI)	<i>P</i> value**
	£/day, mean (sd)		£/day, mean (sd)			
	Baseline	Endpoint	Baseline	Endpoint		
Budget	5.26 ± 1.70	5.58 ± 1.80	5.22 ± 1.57	5.50 ± 1.35	0.09 (-0.93, 1.10)	0.86
Regular 1	6.01 ± 1.94	6.21 ± 1.95	5.92 ± 1.67	6.54 ± 1.50	-0.33 (-1.45, 0.78)	0.55
Regular 2*	5.72 ± 1.87	5.97 ± 1.90	5.66 ± 1.56	6.08 ± 1.41	-0.11 (-1.18, 0.96)	0.84
Quality*	7.78 ± 2.43	7.94 ± 2.57	7.41 ± 2.13	8.00 ± 1.98	-0.06 (-1.53, 1.40)	0.93
Mean all	6.19 ± 1.97	<b>6.43 ± 2.05</b>	6.05 ± 1.72	<b>6.53 ± 1.53</b>	-0.11 (-1.26, 1.05)	0.86

\* factored costs \*\*P value is between groups difference at endpoint, independent samples t-test

Baseline dietary intake categorised into food groups indicated small but significantly higher costs ( $p < 0.005$ ) at baseline in the cardioprotective group for dairy (£0.22/day) and fruit (£0.41/day) reflecting higher intakes, and possibly higher cost choices for these foods, at the start of the intervention. However, the change from baseline in consumption of foods (by weight) in each food group was not different between groups (Table 5.3). There was a significant difference in costs at endpoint between groups for dairy and non-alcoholic drinks, which were higher for the control group, and fish and sugar and snack foods, which were higher for the cardioprotective group. The difference in costs was due to the foods chosen within the food groups, rather than a change in the amount of food consumed within food groups. For example, for the dairy group, the mean difference at endpoint (after accounting for baseline intakes) was 30g/day with the cardioprotective group consuming about two dessert spoons more dairy at endpoint (ns) compared to the control group, but spending £0.33 less per day. Similarly, mean fish intake at endpoint was around 10g/day less in the cardioprotective group compared to control (ns), but the mean daily spend on fish was £0.58 more (Table 5.3).

At endpoint, the top five food groups contributing to the cost of the diet were the same for both groups except for fish, which was in the top five for the cardioprotective group but not the control group, and alcohol, which was in the top five for the control group but not the cardioprotective group (Table 5.4).

Table 5.3 Baseline, endpoint and mean difference in amount and cost of food groups for participants in the cardioprotective and control diet groups

Food Group		Cardioprotective n=20		Control n=20		Mean difference (95% CI) ±	P value±
		Baseline	Endpoint	Baseline	Endpoint		
Cereals and grains	g/day	286.2 (137.0)	300.9 (136.2)	346.4 (150.9)	282.1 (136.1)	-9.7 (-105.0, 85.5)	0.84
	£/day	0.77 (0.48)	0.91 (0.59)	0.93 (0.47)	0.70 (0.32)	0.21 (-0.25, 0.67)	0.36
Dairy	g/day	386.4 (143.5)	355.7 (221.1)	250.0 (119.1)	274.0 (158.1)	30.3 (-111.4, 172.1)	0.66
	£/day	0.65 (0.32)*	0.38 (0.28)	0.43 (0.23)*	0.53 (0.32)	-0.33 (-0.59, -0.08)	<b>0.012</b>
Eggs	g/day	15.1 (21.7)	9.9 (14.8)	17.3 (20.3)	24.6 (22.1)	12.5 (-2.5, 27.5)	0.10
	£/day	0.05 (0.08)	0.04 (0.05)	0.08 (0.09)	0.11 (0.10)	-0.01 (-0.07, 0.05)	0.65
Vegetables	g/day	374.6 (182.8)	446.4 (279.3)	333.9 (158.0)	333.8 (124.2)	-146.0 (-297.9, 5.8)	0.06
	£/day	1.01 (0.58)	0.99 (0.61)	0.88 (0.56)	0.89 (0.40)	0.21 (-0.19, 0.60)	0.29
Fruit	g/day	281.0 (175.7)	298.8 (180.1)	211.2 (221.5)	209.0 (167.8)	-60.2 (-174.7, 54.3)	0.29
	£/day	0.84 (0.68)*	0.81 (0.68)	0.43 (0.42)*	0.56 (0.48)	-0.07 (-0.59, 0.45)	0.80
Nuts	g/day	8.5 (18.1)	8.8 (10.2)	21.5 (46.3)	17.0 (25.1)	2.7 (-11.4, 16.8)	0.70
	£/day	0.06 (0.12)	0.10 (0.13)	0.17 (0.38)	0.12 (0.18)	0.07 (-0.05, 0.20)	0.22
Fish	g/day	49.1 (43.2)	82.2 (61.0)	60.3 (60.8)	48.1 (44.8)	-9.9 (-56.7, 37.0)	0.67
	£/day	0.50 (0.47)	0.99 (0.84)	0.48 (0.44)	0.36 (0.25)	0.58 (0.03, 1.13)	<b>0.038</b>
Meat	g/day	156.4 (111.5)	111.8 (94.5)	198.9 (113.1)	158.3 (112.4)	22.7 (-50.7, 96.0)	0.53
	£/day	1.13 (1.03)	1.02 (1.02)	1.44 (0.95)	1.4 (1.06)	-0.06 (-0.83, 0.71)	0.87
Fats and oils	g/day	19.4 (13.6)	21.4 (11.6)	15.1 (12.3)	18.2 (13.8)	-4.2 (-14.3, 5.8)	0.40
	£/day	0.08 (0.06)	0.08 (0.05)	0.06 (0.05)	0.08 (0.07)	-0.02 (-0.07, 0.03)	0.39
Non-alcoholic drinks	g/day	929.3 (378.4)	1002.5 (533.1)	841.9 (550.5)	913.4 (642.8)	-34.2 (-294.9, 226.4)	0.79
	£/day	0.30 (0.25)	0.20 (0.15)	0.39 (0.41)	0.46 (0.49)	-0.37 (-0.61, -0.14)	<b>0.003</b>
Alcoholic drinks	g/day	157.8 (227.7)	145.3 (258.2)	184.2 (195.5)	191.9 (146.4)	-1.34 (-135.8, 133.1)	0.98
	£/day	0.51 (0.61)	0.46 (0.65)	0.52 (0.71)	0.87 (0.75)	-0.27 (-0.75, 0.20)	0.25
Sugar and snack foods	g/day	26.7 (21.5)	27.5 (14.8)	29.9 (27.5)	29.9 (20.5)	-6.1 (-19.1, 7.0)	0.35
	£/day	0.22 (0.09)	0.36 (0.30)	0.16 (0.16)	0.21 (0.26)	0.22 (0.14, 0.42)	<b>0.037</b>

\* p<0.05, t-test; ± ANCOVA adjusted for baseline intakes; Bonferroni adjustment for multiple comparisons

Table 5.4 Mean cost at endpoint by food group for cardioprotective (CP) and control diet groups

Food Group	CP Ranking	CP £/4days	Control Ranking	Control £/4days	P value
Meat	1	4.07 ± 4.08	1	5.53 ± 4.13	0.269
Fish	2	3.95 ± 3.36	8	1.36 ± 1.04	<b>0.003</b>
Vegetables	3	3.95 ± 2.44	2	3.46 ± 1.61	0.458
Cereals	4	3.62 ± 2.35	4	2.82 ± 1.24	0.189
Fruit	5	3.23 ± 2.70	5	2.17 ± 1.87	0.159
Alcoholic drinks	6	1.82 ± 2.60	3	3.29 ± 3.02	0.107
Dairy	7	1.53 ± 1.12	6	2.06 ± 1.27	0.173
Sugar and snack foods	8	1.45 ± 1.08	9	0.81 ± 1.01	0.058
Non-alcoholic drinks	9	0.80 ± 0.60	7	1.85 ± 1.97	<b>0.037</b>
Nuts	10	0.41 ± 0.52	10	0.47 ± 0.72	0.776
Fats and oils	11	0.31 ± 0.18	12	0.38 ± 0.32	0.374
Eggs	12	0.15 ± 0.22	11	0.41 ± 0.38	<b>0.012</b>

Values are endpoint costs for 4 days intake as recorded in estimated food diaries; mean±SD, P values are from t-tests

## 5.8 Discussion

The key finding of the current study is that a cardioprotective dietary pattern was not more expensive than a control diet representative of the habitual intake of similarly aged people in the UK. These results suggest that cost may not be a barrier to modifying habitual intake to reflect a cardioprotective diet. There was no change in the amount of foods consumed in each of the food groups analysed, however for the cardioprotective group the cost was lower for foods in the dairy and non-alcoholic drinks food groups but higher for the fish and sugar and snack foods groups.

At baseline, food expenditure was comparable to estimates of household expenditure on food and non-alcoholic drinks in England (a mean of £53.30 per week) (Office for National Statistics, 2013c) but much greater than a recent study using similar methods to estimate the dietary cost of foods as consumed by people participating in the National Diet and Nutrition Survey, which reported a mean cost of £2.84 per day for those aged 40–49 years (Timmins et al., 2013a). However this discrepancy may be due to the use of the DANTE food price database, based on 2004 food prices (Timmins et al., 2013b) and not directly comparable with the current study, which used 2013 prices.



Supporting previous findings, the results of this study highlight the variable amounts spent proportionately on food groups with different dietary patterns (Rao et al., 2013). However, although there were differences in actual rankings, the aggregated top five food groups by cost in both groups was remarkably similar, demonstrating only one food group difference in the top five, fish - which ranked second for participants in the cardioprotective group - and alcohol, which ranked 3<sup>rd</sup> in the control group, compared to 8<sup>th</sup> and 6<sup>th</sup> in the respective diet groups. Meat, vegetables, cereal and fruit had different rankings but were all in the top five food groups for spending for both the cardioprotective and control diets.

The difference in spending on fish was highly significant, and can be attributed to the specific advice given to the cardioprotective group to include 1-2 portions of oily fish each week. The finding that - even with increased spending on fish - a dietary pattern approach to dietary change did not lead to greater overall cost of food as selected by free-living individuals, is an important one in an environment of successive years of rising food costs (Office for National Statistics, 2013c).

Greater spending on whole grain cereals has been noted with more health promoting diets (Bernstein et al., 2010) and in this study there was a slightly greater (around £0.80 per day), but not statistically significant, daily spend on cereals in the cardioprotective group. Similarly, the results support a trend for spending more on meat with less healthier diets (Bernstein et al., 2010), but again did not reach statistical significance. Whilst sugar and snack foods appear to be significantly more expensive in the cardioprotective group, this may be an artefact due to attempts to maintain a diet iso-caloric to baseline, as the group were provided with nut cereal bars in this category to replace energy lost in the switch to low fat dairy foods and the avoidance of biscuits and cakes.

Despite the overall group findings supporting a trend towards lower costs in the cardioprotective group when compared to baseline dietary costs, there was variation in how individuals' costs changed across both groups, with some decreasing, others increasing and some staying relatively static. There are a number of potential reasons for this, due either directly to the effect of the dietary interventions or as a result of factors external to the dietary interventions (or a combination of both). For example, the individual changes in cost may reflect the contrast between the baseline diet and the allocated diet with those at baseline more closely resembling the intervention diet than others, experiencing less change in food costs over the 12-week intervention. Differences independent of the study are also likely to have had an influence during the 12 week intervention, as food purchasing behaviour is known to be complex with several potential factors interplaying including social influences (so-called eating 'norms') (Robinson et al., 2013), nutrition information and cues on food labels (Koenigstorfer et al., 2013), pricing strategies (i.e. reduction of prices to increase purchases of a particular food) (French, 2003, Ni Mhurchu et al., 2010, Waterlander et al., 2013), promotional signage (French et al., 2001), taste and, for some, weight or health concerns (Glanz et al., 1998).

The finding of no overall difference in cost contradicts a recent meta analysis of cross-sectional studies which concluded healthier dietary patterns to be more expensive than less healthy patterns (Rao et al., 2013); however this review did not include any studies based on food prices in the UK. Food prices in the UK differ from those of the rest of Europe, and around the world different countries operate under unique market conditions, with international variation in price, taxation, balance of imports and exports, manufacturing and distribution costs affecting food costs (Department for Environment Food & Rural Affairs, 2013). National food cost differences are not static – for example, food prices rose 32% in the UK between 2007-12, but only 13% in the same time period in France and Germany. Thus comparisons are made more difficult when data is across countries and at different time points, notwithstanding the methodological rigour adopted by Rao et al in standardising to a common year US dollar (Rao et al., 2013).

The further finding that there were cost differences associated with some food groups, between the two patterns, highlights the complexity of dietary intakes and the interplay of financial factors potentially affecting food choice. Although cost was different between the two dietary patterns for some food groups, actual consumption (by weight) did not change significantly for any food group indicating that it was a change to the quality of the diet (rather than quantity) that must have prompted the cost change. In the cardio-protective group, total daily costs were significantly higher for fish (due to the encouragement of regular oily fish intake), and for sugar and snack foods (reflecting the provision of wholegrain cereal nut bars for consumption in place of biscuits and cakes); but lower for non-alcoholic drinks and eggs. This is in contrast to the findings of a large prospective cohort study of Spanish university graduates, which found lower daily food costs with higher fish intakes, as well as a variety of less healthy foods and food groups (Lopez et al., 2009). The same study also concluded that vegetables, fruit, wholegrain bread and nuts were associated with higher food costs, which was not confirmed in the present study. This may be due to the larger sample size (and therefore greater power) in the Spanish study, or alternatively the results may be confounded by the costs of food groups being adjusted for energy intake in the study, as healthier diets have consistently been associated with lower energy intakes (Waterlander et al., 2013, Darmon et al., 2003, Drewnowski et al., 2007).

Whilst observational studies largely suggest healthier diets cost more (Cade et al., 2007, Darmon et al., 2007, Aggarwal et al., 2012, Drewnowski and Eichelsdoerfer, 2009), the majority of intervention studies costing actual food intake have shown healthier diets to be no more expensive than control diets (Cleary et al., 2012, Ottelin et al., 2007, Goulet et al., 2008, Raynor, 2002, Burney and Haughton, 2002), in agreement with the present study. However, although intakes were somewhat similar to those reported in the NDNS, the intakes of participants in the cardioprotective dietary intervention study may not reflect those from more disadvantaged backgrounds. They reported higher intakes of fruit, vegetables and whole grains at baseline, for example (Chapter 3). Implementing similar dietary changes in priority groups (i.e. those on lower incomes with poorer health outcomes) could, however, be challenging for a number of reasons – people on lower incomes spend a greater proportion of their income on food overall (Office for National Statistics, 2013c) making them more vulnerable to rising food costs; and the inherent risk of purchasing different foods has a greater consequence if the new food is not popular. Whilst the

cost may not be greater for people with more elastic food budgets, the same may not be the case for those with less flexibility. In addition, there is evidence that those with less money to spend on food are more likely to purchase energy-dense foods with a higher proportion of refined grains, added sugars and fats as an economic strategy to save money (Drewnowski et al., 2007).

The perception that healthier foods are less affordable is frequently cited as a barrier to improving dietary habits (Haynes-Maslow et al., 2013, Williams et al., 2014) despite academic debate as to the validity of the metrics used to cost foods. Consumers are likely to factor in attributes not directly related to cost such as shelf life, spoilage during transport, storage and changes to food quality over time. In this way, fresh apples may be viewed as more expensive than canned apples as they may spoil during transport or storage whereas the canned counterparts retain their quality indefinitely (Haynes-Maslow et al., 2013). For example, whereas academically there is good evidence of an inverse relationship between dietary energy-density and nutrient intakes (Monsivais and Drewnowski, 2009, Ledikwe et al., 2006, Andrieu et al., 2006), the usefulness of pricing foods per energy unit when costing higher quality diets has recently been questioned (Rao et al., 2013). Foods lower in dietary energy for weight - such as fruit and vegetables - have a higher price when measured per energy unit (Carlson and Frazão, 2012) rather than by weight however are generally also of a higher nutrient density (in the form of vitamins, minerals and dietary fibre for example) than foods that have higher calories for weight (Darmon et al., 2005).

## **5.9 Strengths and limitations**

A key strength of the present study is the robustness of the dietary data, taken from 4-day food diaries with detailed information about actual foods consumed, which is not possible to obtain from food frequency questionnaires. The dietary data correlated well with objective biomarkers of dietary intake, and the food price data reflects the cost of diets as actually consumed by the individual participants. Food intake pre- and post-intervention was compared, providing valuable insight into how advice to improve overall dietary pattern affects the food purchasing patterns of individuals. Equal numbers of males and females were included in the sample for costing purposes, increasing the representativeness of the findings.

Several limitations should also be acknowledged. Assumptions made in the costing of food products including package size, brand and availability at each of the supermarkets may not reflect the characteristics of the foods actually consumed by individuals as recorded in diet diaries. For example, it may not be practical for individuals in smaller households to purchase the most economical package size of a food product if such quantities are not able to be adequately stored or consumed by the products' 'use-by' or 'best before' dates. The sample size was small and drawn from the larger sample of participants of the main CRESSIDA study which do not reflect the diversity of social, economic and cultural variation in the wider UK population. Food costs were calculated from 4-day food diaries recorded by participants recruited from multiple cohorts over a two-year period, and there may have been price, food supply and social changes (such as employment and wider economic measures) impacting on food purchase decisions by individuals recruited to the study. Participants were provided with some food pantry items to

assist with compliance to the allocated dietary intervention, and this may have affected other food purchasing decisions – although both dietary interventions were provided with similar food items and quantities so any such influence should have affected both groups equally. Costs were calculated from standard prices and did not take account of discounts or offers (such as ‘buy one get one free’) which are known to influence purchasing decisions (French, 2003). Indirect costs, such as time spent shopping and preparing food, as well as gas and electricity costs, were not included in the calculations when costing individual dietary intake. In addition, the need for food preparation skills, food storage and cooking equipment may have been greater for those participants allocated to the cardioprotective group and these all incur economic costs which have not been accounted for in this study. To understand whether the adoption of a diet consistent with the UK dietary guidelines would be no more expensive for lower income groups, a similar study would need to be undertaken that directly targeted this population.

## **5.10 Conclusion**

In conclusion, a cardioprotective diet based on UK dietary guidelines did not differ in cost from either baseline food costs or the costs of a conventional UK diet. The results do not support the hypothesis that changing to a cardioprotective dietary pattern will be more expensive than a dietary pattern representative of many adults in the UK. The higher cost of fish and snack foods, but not other food groups, for the cardioprotective dietary pattern, is notable. The identification of specific food groups that may be a cost concern for people modifying their habitual intake is particularly useful for nutritionists and dietitians tailoring nutritional interventions for CVD prevention for individuals and populations.

## **Chapter 6 Overall Discussion**

This chapter will summarise the key findings of the studies reported in this thesis, present a brief overview of the findings, describe strengths and discuss limitations of the research program and directions for future research. The main empirical findings of each study in this thesis are chapter specific and were summarised in each of the respective chapters. Each individual chapter compares the respective study results to other findings in the literature, and also discusses the strengths, limitations and meaning of the individual data.

### **6.1 Summary of main findings**

This thesis has explored the efficacy of UK dietary guidelines for the prevention of CVD in middle aged and older adults. The utility of dietary guidelines in terms of their practical implementation into the daily life of participants, and the affordability of such a dietary pattern compared with a conventional UK diet, has also been investigated in order to inform the translation of the study to clinical and public health practice. Both quantitative and qualitative methodology was employed to inform the evidence for population dietary guidance for CVD prevention. Table 6.1 presents an overview of the thesis' hypotheses and objectives.

#### **6.1.1 Cardioprotective dietary pattern informed by dietary guidelines**

Despite a shifting focus away from investigating nutrients in isolation and towards an overall dietary pattern approach, there has not previously been an overall assessment of implementing a dietary pattern consistent with UK dietary guidelines on CVD risk factors. Whilst other studies have focused on the efficacy of dietary patterns in individuals at high risk, this randomised controlled trial (CRESSIDA) explored the impact of an integrated dietary approach in middle aged and older adults of moderate, rather than high risk which is particularly important considering it has been estimated that around a third of cardiovascular events occur in those in the non-hypertensive range (Stamler et al., 1993). The results of this study were presented and discussed in Chapter 3.

The hypothesis that an integrated dietary approach modifying the overall dietary pattern to conform with UK dietary guidelines for the prevention of CVD for a minimum of 12 weeks would lead to significant reductions in daytime SBP and a reduction in TC:HDL-C compared to a conventional UK diet in healthy adults aged 40 to 70 years was confirmed. The results showed an effect of the cardioprotective diet on two of the primary outcomes, with a significant reduction in daytime SBP of 4.2 mmHg and a 4.2% reduction in TC:HDL-C compared to the control diet. However endothelial function, as measured by flow mediated dilation, did not differ between groups. There was a small but spontaneous weight reduction in the cardioprotective group compared to the control group, despite a concerted effort to maintain isocaloric intakes during the intervention. The results were modest but important because they occurred in a population of older adults described as moderate risk rather than high risk.

### **6.1.2 Exploring barriers, motivators and enablers to dietary change**

Whilst dietary and lifestyle behaviours could have a major impact on the health of the UK population, such behaviours are framed by social, cultural and material contexts that are largely ignored in trials of efficacy due to the need to standardise the intervention and approach to behaviour change. Qualitative research can provide important insights into the context and process of an intervention, which have been identified as essential in the transferability of complex interventions but rarely reported (Wells et al., 2012). With translation in mind, eight semi-structured interviews were conducted with participants who had been randomised to the cardioprotective (dietary guidelines) group from CRESSIDA. The results of this study were reported and discussed in Chapter 4.

The objective of this study was to understand the experience of undergoing dietary change during the study and identify factors affecting compliance to the intervention. Motivators identified were sociocultural, and many were specific to the study context (altruism, a belief in science and the experience of participating in a scientific study). Identifying the sociocultural factors likely to motivate a population outside of the study would be important in the translation of CRESSIDA beyond the trial environment. There were however some individual elements identified that could be implemented and transferred outside of a scientific study environment. Provision of food items consistent with the changes recommended, personal incentives and regular feedback on progress could all be considered in the existing primary health context. Many of the barriers identified related to environmental factors as well as the social context, leading to strategies such as avoidance of social situations involving eating, removal of food items inconsistent with the dietary change requested, and a very structured approach to food and eating occasions which would be hard to maintain in the longer term.

### **6.1.3 Investigating the cost of a cardioprotective diet**

Dietary intervention studies are at risk of bias due to the characteristics of those who volunteer – for example people who already have an interest in nutrition may be more likely to volunteer than others without such an interest; likewise those on lower incomes may be less likely to participate in studies than those from higher socioeconomic backgrounds (Galea and Tracy, 2007, Shahar et al., 1996). Socioeconomic differences in knowledge about diet, and differences in the concern about the cost of food have also been documented (Turrell and Kavanagh, 2006), and as the burden of chronic illnesses including CVD is known to disproportionately affect populations of lower income then the cost of a diet consistent with the UK dietary guidelines is an important consideration when determining likely barriers to their adoption in the general population. A retrospective analysis of food records completed by a subset of participants from the CRESSIDA study was therefore undertaken to determine whether the cost of a self-selected cardioprotective diet differed from that of a conventional UK diet (CRESSIDA control diet). The results of this study were presented and discussed in Chapter 5.

The hypothesis that a cardioprotective diet would not be more expensive than a dietary pattern representative of many adults in the UK was confirmed. There was no difference in the cost of the two diets at endpoint, nor was there a difference in dietary costs compared to baseline. There was evidence of a lower cost of foods in dairy foods and non-alcoholic drinks in the group randomised to the cardioprotective diet, however this group also had higher costs for fish and for the 'sugar and snacks' food group. Both groups had remarkably similar patterns in terms of the ranking of the cost of different food groups, with meat, vegetables, cereal and fruit all in the top five food groups for spending for both the cardioprotective diet and control diet groups. These results suggest that, for individuals who are not specifically of lower socioeconomic status, cost may not be a barrier to modifying habitual intake to reflect a cardioprotective dietary pattern. Those from lower socioeconomic groups may however have lower baseline food costs, have less elastic food budgets and spend a greater proportion of their income on food potentially making dietary quality change more challenging especially for those food groups where it was identified that costs were higher for the cardioprotective diet.

Table 6.1 Overview of thesis' hypothesis and objectives

Hypothesis/ Objective	Section discussed	Comment
<p>1. <b>Hypothesis</b> In healthy adults aged 40 to 70 years, modifying the overall dietary pattern to conform with UK dietary guidelines (5 portions of fruit and vegetables per day, increased consumption of whole grain cereals and oily fish; moderate total fat and reduced saturated fat, added sugars and salt intake) will lead to significant changes in the following outcomes after 12 weeks, compared to a conventional UK diet:</p>		
Reduction in daytime systolic blood pressure	Chapter 3	✓ Hypothesis accepted
Reduction in the ratio of total to HDL cholesterol	Chapter 3	✓ Hypothesis accepted
Improvement in endothelial function	Chapter 3	× Hypothesis rejected
<p>2. <b>Aim:</b> To explore the experiences of participants who had been randomised to the cardioprotective diet arm of CRESSIDA.</p> <p><b>Objective:</b> To explore participants' perception of barriers, reinforcing and enabling factors influencing dietary change consistent with the UK dietary guidelines.</p>	Chapter 4	<p><b>Barriers:</b> distrust of packaged foods; food preferences.</p> <p><b>Reinforcing factors:</b> being a study participant, obligation to the study / scientific rigour; benefits of participating i.e. financial, food provided, information about own health, approval of the allocated diet.</p> <p><b>Enabling factors</b> adopting regimented approach; personal skills; changing environment - removing 'temptation'; social and study support.</p>
<p><b>Objective:</b> To explore participants' perception of the advantages and disadvantages of following the dietary guidelines.</p>	Chapter 4	<p><b>Advantages</b> described by participants included some of the reinforcing factors listed above, and also included perceived social, mental and physical benefits.</p> <p><b>Disadvantages</b> incorporated social, mental and physical effects; as well as the process of changing habits and the perceived difficulty of the changes required.</p>
<p>3. <b>Hypothesis</b> A cardioprotective dietary pattern (cardioprotective diet) will not be more expensive than a dietary pattern representative of many adults in the UK (conventional UK diet).</p>	Chapter 5	✓ Hypothesis accepted



## 6.2 Implications of the research

This thesis has demonstrated the efficacy of a diet consistent with dietary guidelines in reducing the risk of CVD, and the potential for a population approach based on dietary change in the UK population. It has also highlighted some of the potential issues in the wider implementation of the dietary guidelines, beyond a trial environment, which identify some of the challenges for changing population dietary norms. The adoption of a 'population' approach, which attempts to shift the mean level of risk of the whole population to a more favourable position, has previously been proposed to be more a more effective approach than an 'individual' (high risk) strategy because (1) it is radical, (2) has the potential for greater risk reduction, and (3) is behaviourally appropriate as it seeks to shift population norms for behaviours that impact on risk rather than a focus on the individual to make changes in a culture that does not support the maintenance of those changes (Rose, 2001).

Cardiovascular disease is a major public health issue, and the prevention of CVD is relevant to a range of important public health guidelines including the most recent Joint British Societies for the Prevention of Cardiovascular Disease (JBS3, 2014), which focuses on shifting the population distribution of risk rather than simply targeting those individuals identified as high risk, and at least six NICE guidance documents (National Institute for Health and Care Excellence, 2006, National Institute for Health and Care Excellence, 2014a, National Institute for Health and Care Excellence, 2010, National Institute for Health and Care Excellence, 2014b, National Institute for Health and Care Excellence, 2012, National Institute for Health and Care Excellence, 2007) which encompass both individual and population recommendations relevant to CVD prevention.

The social, cultural, economic and environmental influences on health have also recently been acknowledged through government reviews, strategies and policies. The Marmot Review *Fair Society Healthy Lives*, commissioned by the UK government, noted significant inequalities in CVD with socioeconomic gradient and identified policy objectives for reducing health inequalities including the creation and development of healthy and sustainable places and communities (UCL Institute of Health Equity, 2010). The Public Health White Paper *Healthy Lives, Healthy People* (Department of Health, 2011a) described a policy of local devolution to empower individuals to make healthy choices and for communities to find unique solutions to address local needs whilst acknowledging the role of the food environment through voluntary industry pledges around five networks (food, alcohol, physical activity, health at work and behaviour change) via the *Public Health Responsibility Deal* (Department of Health, 2011b). The food network pledges encompass enabling individual choice to adopt a healthier diet, the reduction of salt, artificial trans fats and calories in foods sold to the UK population, along with removing the barriers to accessing fruit and vegetables (Department of Health, 2011b).

Whilst the results of CRESSIDA (Chapter 3) support the efficacy of dietary guidelines in CVD risk factor reduction, a dietary approach to prevention will only be effective if it can be implemented on a population basis. Although dietary guidelines have been in existence for many years, the

evidence suggests that the majority of the population do not comply with the advice they contain (Murphy, 2014, Haack and Byker, 2014) and it is important to therefore consider previous work that has explored compliance with dietary advice including population guidance.

Adherence to dietary guidelines is universally poor across a number of countries including the UK, USA and Australia (Srinivasan, 2013, Bates, 2012, Haack and Byker, 2014, Australian Bureau of Statistics, 1999). Factors influencing the uptake of dietary guidelines have generally not been explored systematically or with rigour, and those studies that have been conducted have focused on individual determinants of behaviour rather than social or environmental interventions. For example, quantitative studies of factors influencing compliance have identified those interventions provided at an individual level (Desroches et al., 2013), as well as demographic variables (Bautista-Castano et al., 2004), baseline dietary intakes (Zazpe et al., 2010) and social factors such as marital status or whether they had previously completed a program for dietary change (Desroches et al., 2013, Zazpe et al., 2010). Qualitative investigations have, by contrast, highlighted social, cultural, and environmental factors as important in determining whether an individual adopts dietary change (Khan, 1981, Lappalainen et al., 1997, Wardle et al., 2004), supporting the themes generated in the qualitative study described in Chapter 4.

### **6.3 Shifting the paradigm of dietary change from a simple to a complex intervention for public health**

Complex interventions can be defined according to a range of dimensions including the number of, and interactions between, components within the experimental and control interventions; number and difficulty of behaviours required by those receiving and delivering the intervention; and the degree of flexibility or tailoring of the intervention (Craig et al., 2008). Whereas historically efficacy trials manipulating dietary components have focused on the effect of changing one or two nutrients, the research agenda has moved to study the impact of overall dietary changes, where a cluster of dietary characteristics are combined to form a dietary pattern. This emphasis on dietary patterns, combined with an acknowledgement of the multifactorial nature of dietary change, highlights the complexity of dietary interventions.

Efficacy is one of a number of important criteria by which interventions can be judged in terms of their value in promoting health (Jacobs et al., 2012). The potential for dissemination and adoption of the intervention by the wider population is increasingly being considered as equally essential (Resnicow et al., 2004). Since 2000, the Medical Research Council (MRC) has published guidance for developing and evaluating randomised controlled trials of complex interventions (Craig et al., 2008, Medical Research Council, 2000), and the broader literature reflects a growing trend for a greater understanding of the processes underlying interventions in an effort to inform the development, evaluation and implementation of future interventions in other settings. The call for more robust reporting of published interventions (Hoffmann et al., 2014, Chan et al., 2013, Glasziou et al., 2008) establishes further the recognition of complexity in non-drug interventions, and an acknowledgement that such complexity should ideally be factored into each stage of the research process from planning through to publication (Yao et al., 2013, Chan et al., 2013).

For some time, public health researchers have been calling for trials that extend beyond efficacy and examine the context and effects of interventions delivered under real world circumstances that reflect the complexity of influences on dietary choice in non-trial contexts (Resnicow et al., 2004, Wolff, 2000, Craig et al., 2008, Glasgow and Emmons, 2007). Randomised controlled dietary intervention trials, like CRESSIDA, are essential in demonstrating the impact of dietary interventions in CVD prevention however, by their very nature, the generalizability to other contexts and settings are limited (Glasgow and Emmons, 2007). The use of integrated multiple approaches including qualitative research has been highlighted as useful in strengthening the transferability of gold standard trials to real world settings, but is still not widely adopted (Lewin et al., 2009).

CRESSIDA was a rigorous dietary intervention trial, the methods of which were targeted at changing the dietary choices of the individuals enrolled in the study to reflect the population dietary guidelines of the UK. Importantly these individuals were free to choose their own food intake on a day-to-day basis, but the provision of several incentives were able to overcome some of the social, cultural and environmental barriers including a finite time period in which the dietary changes had to be maintained. Translating the success of CRESSIDA participants to the wider UK population is likely to rely less on targeting individuals to make dietary changes, and more on environmental and social factors, if the potential population benefits of overall reduction in CVD risk are to be realised.

Motivating factors identified in the qualitative study were context-specific, and they enabled participants to change their diet despite the social and environmental barriers that would likely make longer-term dietary change more difficult. Similarly, whilst this thesis has demonstrated that cost was not higher for the participants following the dietary guidelines diet in CRESSIDA, those from different backgrounds in a non-trial setting may have a different experience. In addition the higher costs of some of the more expensive food groups, such as fish and snack foods, may not be as acceptable to lower income groups. As well as cost and nutritional quality, acceptability of dietary change is essential if dietary guidelines are to be successfully implemented. For example, social norms have previously been found to influence mainstream dietary patterns (Maillot et al., 2010), and these may also vary according to ethnic and cultural influences (Karanja et al., 2007) as well as socio economic factors (Maillot et al., 2010).

## **6.4 Strengths and limitations**

The strength of this thesis is that it has tested the effects of an integrated dietary pattern consistent with UK dietary guidelines under gold standard conditions. Importantly, it has also gone on to consider aspects of the translation and implementation of this dietary pattern at a population level. At a time when dietary guidelines are increasingly under scrutiny, the demonstrated efficacy of the UK population guidance is reassuring.

Although gold standard by scientific benchmarks, a limitation when looking at the population level translation of CRESSIDA is that methods more aligned with the MRC Guidance for Developing

and Evaluating Complex Intervention (Craig et al., 2008) were not used. These include the development of the intervention being informed by both a systematic review of the literature and with community input, strong theoretical underpinnings to the intervention, feasibility testing and a pilot phase, and rigorous process evaluation (for example using a framework such as the RE-AIM framework (Glasgow et al., 2001)) to ensure that information about the intervention reach, adoption and implementation was captured to accompany the efficacy outcomes reported. However, in this thesis the addition of the qualitative investigation allowed some identification of barriers, enablers and reinforcing factors to the adoption of dietary change, and the dietary cost study provide a rich source of information that can be used to guide the translation of CRESSIDA outside of the study context.

## **6.5 Conclusion**

Following a dietary pattern consistent with UK dietary guidelines is effective in reducing cardiovascular risk factors. However, the results of the qualitative study suggest a number of factors unique to the study to be instrumental in individual participant compliance, and these factors are unlikely to be present outside of the study context. The cost of the diet was not more expensive than either the baseline or the control diets; however overall cost was higher than that estimated by dietary records from the National Diet and Nutrition Survey. Ensuring the wider uptake of the dietary guidelines in the UK population will require a multi factorial intervention that targets the social, cultural and environmental factors influencing dietary intake, as well as individual knowledge, skills and attitudes.

## **6.6 Future investigations**

Inevitably, dietary research is increasingly being recognised for its complex nature and the future of CRESSIDA is in testing its translation to a population less motivated by altruism and more heterogenous. Given that hard to reach communities are disproportionately affected by CVD (Bambra et al., 2009b), it would be useful to extend the study to these groups – including those of low income and education, as well as individuals who may not benefit from mainstream public health nutrition messages, such as those who may be physically or intellectually disabled. An investigation into the cost implications of dietary change in these groups is also warranted. Further research is needed to develop a multi-pronged public health intervention that captures financial, social, cultural and environmental influences on dietary behaviour with a rigorous process evaluation underpinning implementation. Both qualitative and quantitative research methods would provide useful evidence for both the efficacy and effectiveness on a population level.

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## Appendix 2.1 Biomarkers of dietary intake

### Introduction

Dietary assessment methods are known to incorporate random and systematic errors, often considerable (Jenab et al., 2009, Bingham, 2006, Prentice et al., 2013) and these make accurate estimates of dietary intake difficult even when a standardised and rigorous approach is adopted (Tucker et al., 2013). The limitations of dietary assessment are well known and documented (Beaton et al., 1997, Kipnis et al., 2002) but true validation of dietary assessment methods is not possible as independent observation of food intake in free living conditions is not viable and all available methods rely on reported data (Bingham, 2006). As well as data reporting issues, the analysis of reported data is subject to a variety of interpretations including food preparation method and portion size, as well as the limitations of nutrient composition data.

Biomarkers of nutritional intake seek to overcome the errors inherent in dietary assessment data (Prentice et al., 2013). These can be blood, urine or other biological samples which can reflect nutritional intake sufficiently closely to be considered an objective marker of true intake (Bingham, 2006). There are a number of considerations involved in selection of nutritional biomarkers, including a suitable temporal relationship with the dietary intake, biological confounders, within-subject variation, sample collection, transport and storage, and analytical measurement errors. Ideally, biomarkers should be objective measures that are independent of dietary intake, such as doubly labelled water or 24 hour urine collections (Arab and Akbar, 2006, Blanck et al., 2003). To be useful, a robust methodology to accurately quantify the biomarker should be available, the concentration of the biomarker should be sensitive to changes in usual dietary exposure, and should be specific to the intake of the nutrient of interest (Andres-Lacueva and Zamora-Ros, 2010). Methodological aspects should address the measurement itself (including sample collection) as well as its interpretation, incorporating validity (representative of true value), precision (repeatability), sensitivity (identifies individuals with intake of the nutrient) and specificity (identifies individuals without intake of the nutrient) (Blanck et al., 2003).

Although objective, biomarkers are complementary rather than a replacement for dietary assessment methods, as they do not only reflect dietary intake but also reflect physiological processing and storage of the nutrient being assessed. Thus they have limitations of their own, including inter-individual variability in absorption, transport, uptake, metabolism and excretion (Arab and Akbar, 2006, Blanck et al., 2003). It is recommended that biomarkers used to validate dietary assessment methods for particular nutrients are calibrated under controlled conditions (Bingham, 2006, Prentice et al., 2013). Biomarkers have particular utility where they validate nutrients known to be poorly assessed through dietary assessment (Schachter et al., 1980) – for example salt intake which is consumed in small amounts in the diet, is widely added to manufactured products in amounts that vary widely from brand to brand (Mattes and Donnelly, 1991), and has been subject to manufacturer changes in recent years such that historical food composition tables are not accurate.

## Methods used in CRESSIDA

A number of biomarkers were measured, and a summary for each of the dietary and nutrient targets is presented in Table 1.

Table 1: Summary of biomarkers used as objective measure of target foods and nutrient

Food/ nutrient	Biomarker used in cardioprotective dietary study
Salt	Urinary sodium
Fruit and vegetables	Urinary potassium
Added sugars	Urinary sucrose and fructose
Whole grains	Serum alkylresorcinol Serum folate
Oily Fish	Total erythrocyte phospholipid fatty acid composition (n-3 long chain PUFA)

## Method of urinary collection for biomarkers

Twenty-four hour urine samples were collected at five timepoints: two at baseline (Week -2, 0), and three at weeks 4, 8 and 13 weeks of the intervention. Timing of collection aimed to coincide with dietary assessment. A urine collection protocol was developed based on standardised methods used in previous studies (Sadler et al., 2012). Participants were asked to collect all urine from the second pass of the day until the first pass of the following day in 2.5 litre bottles containing boric acid as a preservative. They were asked to take 3 x 80g para-aminobenzoic acid at three regularly spaced intervals throughout the day, with the first being taken after the first urine pass and before the urine collection was started.

Urine samples were returned either personally by participants or by courier. When couriered, participants were asked to mark with a permanent pen the meniscus of the urine and then carefully transfer 10 ml aliquot from each bottle using a 10 ml Urine Monovette (Sarstedt, cat no 10.252), labeled with the relevant bottle number. The remaining urine was then disposed of and the Urine Monovette(s) containing the urine aliquot(s) and empty urine bottle(s) marked with the urine meniscus were returned. Upon receipt, the total urine volume was recorded and 7 x 1.5 mL aliquots of pooled 24h urine samples were stored at -80°C until analysis. Samples were sent in batches, over four cohorts (Cohort 1: August – December 2010; Cohort 2: January – June 2011; Cohort 3: July – December 2011; Cohort 4: January to June 2012) to the Clinical Chemistry Department at King's College Hospital for analysis.

Completeness of urine collection was measured using recovery of para-aminobenzoic acid according to a standard protocol (Bingham and Cummings, 1983). Total urine volume for each sample was calculated and 7 x 1.0ml aliquots were removed and stored at -20°C until analysis. Analysis of samples was conducted at the Department of Clinical Biochemistry, King's College Hospital. Para-aminobenzoic acid clearance analysis was undertaken in the laboratory of the Diabetes and Nutritional Sciences Division at King's College London at the end of the study.

## **Urinary para-amino benzoic acid (PABA) analysis**

Urinary PABA was analysed by a colorimetric technique based on previous reports (Bingham and Cummings, 1983). 100 µL sample or blank was incubated in 4 mL 2M NaOH solution at 100 °C for 2 hours. After cooling, 1.5 mL 10M HCl was added followed by 0.5 mL each of sodium nitrite solution, then ammonium sulphamate solution, then naphthylene ethylene diamine solution, allowing at least 2 minutes after each addition. After incubation at room temperature for 1 h, 50 µL of the mixture was transferred to a microassay plate for spectrophotometric absorbance analysis at 540 nm using a plate reader.

## **Biomarker of salt intake**

Compliance to the advice to reduce dietary salt was assessed by 24-hour urine collections on five occasions: two at baseline (prior to Visits B and C), and three on intervention at weeks 4, 8 and 12. Twenty-four hour sodium excretion was determined using an indirect ion selective electrode on the ADIVA 2400 analyser (Sieman's Healthcare Diagnostics, Frimley, Surrey, UK). Samples were diluted in ISE buffer (1:33 dilution) to provide a constant pH and a constant ionic strength solution. As the buffered sample flowed past the electrode a new equilibrium formed due to selective ion transport at the electrode surface resulting in a change in measured potential difference in the cell. This electrical potential was measured against a reference electrode and was logarithmically related (via the Nernst equation) to the sodium concentration in the sample. Completeness of urine collection was assessed by the recovery of paraminobenzoic acid (PABA) in the urine as previously described (Sadler et al., 2012, Bingham and Cummings, 1983).

Urinary excretion serves as a proxy marker of sodium intake as data from food records is limited or unreliable (Schachter et al., 1980) and is the method used in the UK National Diet and Nutrition Survey (Sadler et al., 2012). Urinary sodium was expressed in mmol/ L and converted to equivalent grams of dietary salt by calculating one gram of salt for each 17.1 mmol of sodium recovered in the urine, assuming all of the sodium was derived from salt.

## **Biomarkers of fruit and vegetable intake**

Compliance to advice to consume 5 portions of fruit and vegetables per day was measured by 24 hour urine collections on five occasions: two at baseline (prior to Visits B and C), and three on intervention at weeks 4, 8 and 12. Urinary potassium was analysed by indirect ion selective electrode (ISE) on the ADIVA 2400 analyser (Sieman's Healthcare Diagnostics, Frimley, Surrey, UK). Samples were diluted in ISE buffer (1:33 dilution) to provide a constant pH and a constant ionic strength solution. As the buffered sample flowed past the electrode a new equilibrium formed due to selective ion transport at the electrode surface resulting in a change in measured potential difference in the cell. This electrical potential was measured against a reference electrode and was logarithmically related (via the Nernst equation) to the potassium concentration in the sample. Completeness of urine collection was assessed by the recovery of paraminobenzoic acid (PABA) in the urine as previously described (Sadler et al., 2012, Bingham and Cummings, 1983).

Urinary excretion is the gold standard for assessing potassium intake, with 85-89% of intake is excreted in urine (Bingham et al., 1997, Bingham, 2006) and is strengthened further by the variety of foods in the diet containing potassium, including fruit and vegetables. Urinary potassium was expressed in mmol/L and there are no specific conversion factors for translating urinary potassium to portions of fruit and vegetables.

## **Biomarkers of added sugars intake**

Compliance to advice to reduced intake of added dietary sugars was assessed by measuring urinary sucrose and fructose on three occasions – once at baseline and twice during follow up. Samples were analysed in one batch at the end of the study by the Clinical Chemistry Department at King's College Hospital. Urinary sucrose and fructose were analysed using a liquid chromatography – mass spectrometry (LC-MS) method. Samples were prepared by adding 700 µL of acetonitrile and 100 µL of internal standard solution (approximately 10 µL each of  $^{13}\text{C}_{12}$ -sucrose and  $^{13}\text{C}_6$ -fructose, Cambridge Isotopes Inc, Andover, USA) to 200 µL sample then vortex mixing for one minute. Following centrifugation, the supernatants were analysed by LC-MS on a Jasco <sup>TM</sup> LC2000 series HPLC system attached to a API 3200 <sup>TM</sup> triple quadrupole mass spectrometer (Applied Biosystems, Cheshire, UK) using an apHera NH2 polymer analytical column (250 x 4.6 mm, particle size 5.0 µm, Sigma-Aldrich, Poole, UK) operated in interaction LC HILIC mode. Inter-assay CVs were 3.7%, 8.3% and 4.2% for fructose and 7.4%, 7.9% and 6.7% for sucrose for the low, medium and high quality control samples respectively.

Urinary excretion of sucrose and fructose have previously been found to be associated with dietary sugar intake, and in particular added (extrinsic) sugar in the diet (Tasevska et al., 2005, Tasevska et al., 2009). Unlike urinary potassium, urinary sugars excretion is low compared with intake, and so is less established as a biomarker. It does provide a higher correlation with intake in a dose response manner, and is highly predictive of dietary added sugars intake (Tasevska et al., 2009). Results of the assays are reported in µmol/24 hours.

## **Biomarkers of whole grain intake**

Changes in serum folate and alkylresorcinol concentrations were used to assess compliance to increased intake of wholegrain cereals. Serum folate and plasma alkylresorcinols were measured at baseline and endpoint.

Serum folate was analysed on the ADVIA Centaur Immunoassay System using the Advia Centaur folate assay (Sieman's Healthcare Diagnostics, Frimley, Surrey, UK), a competitive immunoassay in which the sample is pretreated to release the folate from endogenous binding proteins. The released folate competes with acridinium ester-labeled folate for a limited amount of biotin-labeled folate binding protein. Biotin-labelled folate binding protein binds to avidin that is covalently coupled to paramagnetic particles in the Solid Phase. The sample folate concentration is inversely proportional to the amount of relative light units (RLUs) detected by the system. Inter-assay CVs were 6.11%, 7.19% and 6.36 % and intra-assay CVs were 7.93%, 4.54% and 6.26% for low, medium and high quality control samples respectively.

Plasma alkylresorcinol concentrations were determined by capillary gas chromatography – mass

spectrometry (GC-MS) analysis based on a previously described method (Landberg et al 2009) on plasma samples collected into EDTA coated tubes. 400  $\mu$ L plasma sample containing 20  $\mu$ L internal standard (1000 ng/ml C20:0 alkylresorcinol, Reseachem AG, Burgdorf, Switzerland) was incubated in 1 ml 50% ethanol solution for five minutes. The mixture was extracted into 2 x 2mL diethyl ether and the pooled organic extracts were dried under air then re-solubilized into 1 mL methanol. The extracts were purified by loading onto solid phase extraction cartridges (Oasis MAX 3 $\mu$ m /60mg /3mL cartridges, Waters Ltd) primed with 1 mL 0.1M sodium hydroxide (NaOH) in 70% methanol solution. The cartridges were washed with 2 mL methanol then dried under vacuum, after which alkylresorcinols were eluted with 2 mL 2% acetic acid in methanol solution then dried by centrifugal evaporation. To derivatise prior to analysis, 25  $\mu$ L BSTFA and 25  $\mu$ L acetonitrile were added to the dried purified eluent and after standing for at least 30 minutes at room temperature, were analysed by GC-MS (Agilent Technologies HP 6890 series GC oven system with HP5973 mass selective detector).

## **Biomarkers of oily fish intake**

Compliance to advice to increase portions of oily fish (n-3 long chain polyunsaturated fatty acids) was assessed by changes in erythrocyte phospholipid and plasma fatty acid composition, measured at baseline and endpoint. Erythrocyte phospholipid fatty acid composition has been shown to be a reliable biomarker of dietary docosahexaenoic acid (22:6n-3) and eicosapentaenoic acid (20:5n-3) (Serra-Majem et al., 2012).

Erythrocyte membrane phospholipid fatty acid composition was determined as previously described (Sanders et al., 2006). Erythrocytes collected into EDTA coated tubes were washed with saline and lipids were extracted with a mixture of isopropanol chloroform containing butylated hydroxyl toluene (50 mg/L) as an antioxidant. The lipid extract was stored at  $-40^{\circ}\text{C}$  until analysis. Prior to analysis, solvent was removed in a centrifugal evaporator and the lipid extract was transesterified with sodium methoxide in methanol to yield fatty acid methyl esters which were separated and quantified by gas chromatography (Agilent Technologies, UK) using a BP70 capillary column (SGE, Milton Keynes). Previous studies have demonstrated there is no significant deterioration in frozen lipid extracts for the time period involved (Sanders et al., 2006). Plasma total fatty acid composition was determined following interesterification of plasma with methanolic HCL and gas chromatography (Sanders et al., 2006).

Results are expressed as percent of weight of total fatty acid methyl esters.

## **Analysis of fasting blood samples for biomarkers of intake**

Plasma folate was analysed at the end of each cohort by the Clinical Chemistry Department at King's College Hospital, which is CPA accredited. Plasma alkylresorcinols and erythrocyte lipid fatty acid composition were analysed following in-house procedures at the end of the study in the Diabetes and Nutritional Sciences Division, King's College London. All samples were batch analysed, with samples for each subject analysed consecutively in the same run in order to minimize inter-assay variability.



## Appendix 2.1 References

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## **Appendix 3.1 Written dietary information provided to participants**

### **Dietary information provided to participants randomised to cardioprotective dietary arm**

1. Your questions answered (2 pages)
2. Summary overview of dietary changes (2 pages)
- 3 Detailed dietary information by food group (11 pages)
- 4 Label reading (4 pages)
- 5 Eating out and convenience meals (6 pages)
- 6 What is a portion of fruit and vegetables? (2 pages)
- 7 Which fish is oily? (1 page)
- 8 Summary of changes (to be completed by participant)

## **SOME OF YOUR QUESTIONS ANSWERED**

Thank you for volunteering to take part in the CRESSIDA study. Please take the time to read the enclosed leaflets, which give you advice on the changes we will be asking you to make to your diet during the study.

### **Why are we asking you make changes to your diet?**

Previous studies have looked at what happens to your risk of heart disease when you change one aspect of your diet. The aim of this study is to find out if making a number of changes to your diet in combination reduces your risk of heart disease or stroke, compared with a balanced traditional British diet.

This is not a weight loss study and you are free to eat as much or as little as you wish of other foods. We will examine whether specific changes in the types of food you eat can improve your health.

### **Why is it important that I make the changes to my diet?**

It is now widely recognised that there are links between what we eat and our health. This research project will provide important guidance on the types and quantities of foods we should be eating to improve health. We recognise that the success of the study is wholly dependent on people, like you, volunteering their time to take part. However the results we obtain will only be useful to public health recommendations if we can be sure that the dietary changes we ask you to make have been followed.

### **What support will I receive to help me follow this dietary advice?**

We will help you to follow your dietary advice by providing a number of foods we would like you to introduce into your diet. If you are unable to eat the foods we provide it is important to tell us and we will try our best to offer alternatives so that you may be able to continue to take part.



## **What changes will I have to make to my diet?**

The study will be comparing two different diets – a ‘modern’ view of a healthy diet and a more traditional view of a healthy diet. You have been allocated to a group that will follow one of these diets; this was a random process meaning that you had an equal chance of being allocated to either one of the two groups. These guidelines are specific to the group to which you have been allocated. Both of the groups are equally important to the findings of the study.

We will be asking you to eat certain foods in particular quantities, these are everyday foods and do not contain any unusual ingredients and will replace similar foods that you are likely to eat as part of your normal diet. In addition we will be asking you to avoid certain foods that you may or may not regularly eat. These changes to your diet will ensure that the types and amounts of food and nutrients in your diet match the requirements of the group to which you have been allocated. During the study we will ask you to make changes to your consumption of the following foods, some of which we will provide for you.

1. Fats - spreads and cooking oils
2. Snacks
3. Milk and milk products
4. Breakfast cereals
5. Rice/pasta /potatoes/ bread
6. Fish



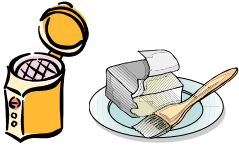



You will need to continue with these changes for the whole 12 weeks of the study.












## **What if I have questions or I am having trouble following the advice?**

We want to make it as easy as possible for you to follow your dietary advice. We are available to answer your questions by phone or email. If you are unable to eat the foods we provide or have other problems which affect your ability to make the changes we have asked, it is important to tell us.

Phone numbers: 020 7848 3360 or 020 7848 4461.

Email: [cressidastudy@kcl.ac.uk](mailto:cressidastudy@kcl.ac.uk)

<b>CRESSIDA</b> <b>Changes</b>	 <b>Choose these....</b>	 <b>Avoid these....</b>
<p><b>Fats</b></p> 	<p><input type="checkbox"/> Use the <b>study</b> spread instead of butter or margarine: <i>in sandwiches, on vegetables, in sauces and in baking.</i>  <b>Aim for 2- 4 teaspoons each day</b></p> <p><input type="checkbox"/> Use the <b>study</b> oil instead of your usual cooking oil or as a vinaigrette  <b>Aim for 1-2 tablespoons each day</b></p>	<p><input type="checkbox"/> Butter, other spreads</p> <p><input type="checkbox"/> Your usual cooking oil</p>
<p><b>Sugar</b></p> 	<p><input type="checkbox"/> Water and sugar free drinks</p> <p><input type="checkbox"/> Use fruit or artificial sweeteners instead of sugar</p>	<p><input type="checkbox"/> Regular soft drinks, juice drinks</p> <p><input type="checkbox"/> Sugar</p> <p><input type="checkbox"/> Sweet processed foods</p>
<p><b>Snacks</b></p> 	<p><input type="checkbox"/> Fresh fruit</p> <p><input type="checkbox"/> Low fat yoghurts and custards</p> <p><input type="checkbox"/> Nuts, Nut cereal bars</p> <p><input type="checkbox"/> Oat, corn or rice cakes</p> <p><input type="checkbox"/> Raw vegetable sticks with reduced fat hummus or yogurt based dips</p>	<p><input type="checkbox"/> Cakes, Biscuits, Crackers</p> <p><input type="checkbox"/> Chocolate, sweets</p> <p><input type="checkbox"/> Crisps, olives, fried snacks</p>
<p><b>Salt</b></p> 	<p><input type="checkbox"/> Fresh foods or processed foods that are lower in salt</p> <p><input type="checkbox"/> Use herbs and spices, lemon, vinegar or pepper instead of salt</p> <p><input type="checkbox"/> Home cooked soups and sauces that have little or no added salt</p> <p><input type="checkbox"/> Choose reduced salt versions of shop bought products and keep portions small</p>	<p><input type="checkbox"/> Processed foods high in salt</p> <p><input type="checkbox"/> Added salt in cooking and at the table</p> <p><input type="checkbox"/> Shop-bought soups, gravies and sauces (including ketchup) that are high in salt</p> <p><input type="checkbox"/> Pickles</p>

<b>CRESSIDA Changes</b>	 Choose these....	 Avoid these....
<b>Fruit and vegetables</b> 	<input type="checkbox"/> At least 2-3 portions of fruit a day <input type="checkbox"/> At least 2-3 portions of vegetables a day	<input type="checkbox"/> Processed potato products ie: shop bought chips, waffles, wedges, or crisps
<b>Meat, fish, chicken and alternatives</b>   	<input type="checkbox"/> At least two portions of fish a week, with one or more being oily fish. Fresh oily fish or fish canned in sunflower oil or spring water. <input type="checkbox"/> White fish and shellfish <input type="checkbox"/> Chicken and turkey without skin <input type="checkbox"/> Beans and pulses: these can also be used to extend small amounts of meat in casseroles, stews and pasta sauces <input type="checkbox"/> Fresh lean cuts of meat	<input type="checkbox"/> Processed meats ie: bacon, sausages, hot dogs, ham and cold cuts of meat <input type="checkbox"/> Fatty meats ie: pate, burgers, some minced beef and lamb <input type="checkbox"/> Salted meat products ie: boiled beef/ brisket, & corned beef <input type="checkbox"/> Salted fish and shellfish <input type="checkbox"/> Meat in pastry ie: sausage rolls, meat pies, pork pies, pasties.
<b>Milk and milk products</b> 	<input type="checkbox"/> Low fat dairy products: skimmed milk, low fat yogurt, low fat fromage frais. <input type="checkbox"/> Choose cheese with a lower fat content. No more than 3 small portions (the size of a small matchbox) per week.	<input type="checkbox"/> Full fat dairy products: full cream milk, yogurts, fromage frais, cheeses
<b>Breads and starchy foods</b>    	<input type="checkbox"/> Wholegrain breads: granary, multigrain and wholemeal breads <input type="checkbox"/> Wholegrain Breakfast cereals ie: Jumbo Oat Porridge, Oatibix, Sainsbury's fruit and nut muesli, Mini Wheats <input type="checkbox"/> Wholegrain crackerbreads, rice/ corn/ oat cakes. <input type="checkbox"/> Cous cous, polenta, scotch barley, quinoa <input type="checkbox"/> Brown rice and wholemeal pasta <input type="checkbox"/> Fresh potatoes prepared with the study oil or spread, and little or no salt <input type="checkbox"/> Oven chips with no added salt	<input type="checkbox"/> White bread, rolls, naan breads <input type="checkbox"/> White rice and pasta <input type="checkbox"/> Processed and sugar sweetened breakfast cereals

## Fruit

Aim to include at least **2-3 portions** of fruit each day

- ☑ Fresh fruit is a better choice than fruit juice. Dried, frozen and tinned fruit (not canned in syrup), drained of juice, can also be eaten.



- ☑ Aim to include at least **two to three portions** of fruit every day.

*For example:*

Raspberries on your cereal in the morning

Plus

A banana for an afternoon snack

Plus

A small bowl of fruit salad for dessert.



- ☑ As a 'rule of thumb' a portion of **fresh fruit** is roughly what would fit in the palm of your hand.

Examples:

One medium apple

Two apricots

A handful of grapes

One medium banana

**Dried fruit** should be eaten in smaller portions, for example one portion is:

Three whole dried apricots

One tablespoon raisins

One heaped tablespoon currants or sultanas or mixed fruit

Two dried figs

Three dried prunes

**Fruit juice** counts as one portion no matter how much you have. Keep fruit juice to a maximum of one small glass per day.

## Vegetables

Aim to include at least **2-3 portions** of vegetables each day

- ☑ Aim to have at least **two to three portions** of vegetables (not including potatoes) every day.

For example:

A small salad at lunchtime.

Raw peppers, carrots and celery & yoghurt or hummus dips.



Adding salad vegetables to sandwich fillings.

Adding vegetables to curries, stews and casseroles.

Filling your dinner plate with a variety of different vegetables.



- ☑ Vegetables can be fresh, frozen or canned. Where vegetables are canned, try to choose those labeled as 'no salt' or 'reduced salt'.

- ☑ As a 'rule of thumb' a portion of cooked vegetables is roughly what would fit in the palm of your hand. For uncooked vegetables, such as salad vegetables, a portion is slightly more. Examples:

Three tablespoonfuls of cooked carrots or peas

Two medium broccoli florets

Three tablespoonfuls of sweet corn

Three tablespoonfuls of kidney beans

One cereal bowl of mixed salad

Three sticks of celery

Seven cherry tomatoes



## Bread and starchy foods

Include starchy foods at every meal.

- ☑ Choose freely from the following lower salt alternatives to bread such as:

- ✱ Brown rice (microwaveable brown rice will be provided to you, this cooks in 3 minutes)
- ✱ Wholemeal pasta
- Jacket and new potatoes, use only study oil or spread and no salt in the preparation
- Oven chips with sunflower oil and no added salt  
Examples:  
McCain Oven Chips  
Waitrose Organic Straight Cut Oven Chips

- ☒ Avoid processed potato products, which are often cooked in the wrong type of fat and have too much salt added. *These include shop bought chips, chips and wedges with coatings, potato waffles and crisps.*

- Cous cous

- ✱ Bulgher/ Bulgur wheat (for example **tabbouleh**)

- ✱ Polenta (cornmeal)

- ✱ Dehulled barley (Scotch barley)

- Quinoa (seed)

- ✱ Ryvita crispbreads, oat cakes, rice cakes and corn cakes, particularly the 'natural flavour' types, are also suitable alternatives.

Wherever possible, choose **whole grain** breads, preferably those that are lower in salt.

Examples of suitable breads are:

- ✱ Pumpernickel bread
- ✱ Hovis wholemeal sliced bread and wholemeal rolls
- ✱ Burgen wholegrain and cranberry sliced bread
- ✱ Kingsmill tasty wholemeal sliced bread and tasty wholemeal rolls

✱ Kingsmill Oatlicious ® sliced bread

✱ Wholemeal mini pitta bread

✱ Chapattis, made with wholemeal atta (flour)

○ Wholemeal lavash breads

☒ If you prefer to make your own bread in a breadmaker, try one of the **recipes** provided.



## Breakfast Cereals

Aim for one portion of breakfast cereal every day

- ☑ Try to have breakfast everyday. Cereal with skimmed milk (red top) and fresh fruit is an example of a healthy breakfast.
- ☑ Choose a wholegrain cereal, that is lower in sugar and salt. Recommended breakfast cereals are:

### 🌿 Jumbo oats\*

- Cook the oats without added salt.
- Add no more than a teaspoon of sugar or honey per serving.
- Add grated apple and cinnamon for flavour and sweetness; unroasted nuts can also be added for extra crunch.
- Top with a yogurt and fresh fruit to add sweetness.

### 🌿 Shredded wheat\*

### 🌿 Oatibix\*

- Add no more than a teaspoon of sugar or honey per serving.
- Add a portion of dried fruit (eg a tablespoon of raisins) or try topping with a yogurt and fresh fruit for sweetness.

### 🌿 Sainsbury's luxury fruit and nut muesli\*

- Do not add any sugar or honey to this cereal, it is sweet enough!
- This is a sweeter cereal, with the sweetness coming from dried fruit.
- Yogurt and fresh fruit can still be added.

\* These cereals will be provided for you.

Aim to include 2-3 serves of low fat milk and dairy products each day

## Milk and dairy foods

- ☑ Use only skimmed (red top) milk. Include milk in cereal, tea and coffee, other drinks, and puddings.
- ☑ Remember to ask for low fat milk when you buy drinks, for example coffee, caffè latte.
- ☑ Include low fat yogurt daily, choose those with 3% or less fat and minimal added sugars.

Examples of suitable yogurts include:

- Ski low fat fruit yogurts
- Muller Light yogurts
- Activia fat free yogurts
- Rachels Organic low fat yogurts
- Sainsbury's Low Fat French Recipe Yogurts
- Shape Zero yogurts (NAS)

- ☑ Choose lower fat dairy products for puddings and desserts; try to have these with fruit.

Examples include:

Make your own custard using skimmed or 1% milk.

Ready made custards with less fat and sugar are also suitable eg Sainsbury's Be Good to Yourself Custard.

Choose lower fat frozen yogurt, sorbets or iced dessert.

- ☑ Limit cheese to a small portion (a small matchbox) no more than three times per week. Choose those that are lower in fat and salt where possible.

Examples include:

- Quark
- Fromage frais, plain Babybel and Babybel Light cheeses
- Sainsbury's Bavarian Smoked Cheese
- Kerry Low Low Mature Cheese Slices
- Philadelphia Light and Philadelphia Extra Light cream cheese
- Fresh mozzarella
- Sainsbury's soft cheese, Be Good To Yourself
- Low fat cottage cheese (eg Sainsbury's Be Good To Yourself, Tesco Light Choices) – plain or pineapple

- ☑ Note that some cheeses are particularly high in salt. These include blue cheeses, edam, feta, gouda, parmesan.

- Use these cheeses in small amounts or when eating low salt foods such as fresh salads and vegetables prepared without salt

## Meat, Chicken and Alternatives

Include meat and chicken up to three times a week

- ☑ Eat fresh meats rather than processed meats (such as hot dogs, sausages, salamis, and burgers) wherever possible
- ☑ Choose leaner cuts and trim all visible fat from meat
  - Turkey and chicken breast, particularly without skin, are lower in fat than other meats
  - Look for lean pork cuts, for example pork medallions (3g fat/100g), which are a better option than standard pork loin (7.6g fat/100g)
  - Choose lean cuts of lamb and beef, and limit these to once per week
- ☑ Avoid meat products in pastry, including pies, pasties and sausage rolls
- ☑ Avoid fatty meats including pate, burgers, some minced beef and lamb
- ☑ Avoid salted meats, such as gammon, bacon, ham and corned beef
- ☑ Avoid meat products in pastry, including pies, pasties and sausage rolls
- ☑ Eggs may be included as an alternative to meat and chicken, in moderation
- ☑ Beans and pulses, such as kidney beans, lentils, chickpeas and baked beans, are a good alternative to meat one or two days a week. They can also be used to reduce the amount of meat in casseroles, stews and pasta sauces.



## Fish and Shellfish

Include **at least two** portions of fish each week, with one or more being oily fish.

- ☒ Include fish in place of meat at least twice a week.
- ☒ Fresh<sup>#</sup> or tinned fish\* is fine; if buying tinned fish purchase the kind tinned in spring water or sunflower oil.
- ☒ Different types of fish are classified as 'white fish' or 'oily fish'; both types are good to include but you should ensure that one of your weekly portions is an oily fish.
- ☒ Oily fish includes fish such as salmon, mackerel, sardines, trout and herring. **Include at least one portion of oily fish a week.**

- ☒ White fish includes fish such as haddock, plaice, pollack, coley and cod.
- ☒ Shellfish is also a healthy choice, for example mussels and langoustines.
- ☒ Take care to avoid high fat high salt sauces – stick to lemon juice and pepper, or other herbs.
- ☒ Some fish and shellfish is higher in salt. These include smoked haddock, kippers, and prawns.
  - Eat these in smaller portions and with foods that are lower in salt such as fresh salad and vegetables cooked without added salt.

\* You will be provided with tinned mackerel or sardines.

<sup>#</sup>You will be reimbursed for fresh oily fish, please keep your receipts.

## Snacks

- ☑ Snacks can be included every day, provided they are healthier choices.
- ☑ Try to match portions with your hunger rather than just finishing the whole packet.
- ☑ Limit your intake of chocolate, sweets, biscuits, cakes, crisps and fried snacks.
- ☑ Olives, pickles, salted nuts should be limited or avoided, as they are very high in salt.
- ☑ Snacks based on nuts, wholegrains, fresh fruit and low fat dairy products can be included daily.

### Savoury snack suggestions

- ☀ Home made popcorn (see recipe, it takes only a few minutes and is much healthier than prepackaged microwave popcorn)
  - Small serve 10-20g of unroasted unsalted nuts eg macadamia nuts\*, almonds\*, hazelnuts
  - Paterson's Cheese & Chilli Oat Bites (limit to one portion per day)

- ☀ Whole grain rice or corn cakes, for example Kallo Original or Sesame Rice Cakes; Real Foods Corn Thins
- ☀ Snack A Jacks lightly salted popcorn (NB other Snack A Jacks varieties are very high in salt or sugar)

### Sweet snack suggestions

- Fresh fruit cut up into bite size pieces or made into a fruit salad. For example:
  - Cut up pineapple chunks with fromage frais
  - Handful of grapes or cherries
  - Mixed berries: raspberries, blueberries, strawberries with frozen yogurt
- Low fat yogurts and custards (see milk section)
- ☀ Nut cereal bars\*
- Smoothies made with skimmed or 1% milk and blended with fresh fruit and yogurt

\* These products will be provided to you.

## Drinks

### Non-alcoholic Drinks

- ☒ Enjoy water; it is a healthy choice for quenching your thirst. Add a slice of lemon or lime, or a splash of fruit juice, for flavour.
- ☒ A small glass of 100% **fruit juice** with a meal can be included each day.
- ☒ Avoid all fizzy drinks, squashes, juice drinks, energy drinks as they contain a lot of sugar. Low sugar ('diet' or 'Lite' versions of these drinks can be included.
- ☒ You may drink tea and coffee, provided they are not the only drink you have.
  - Take care to use skimmed milk only particularly in drinks containing large amounts of milk such as cappuccinos and lattes.
  - If you have more than 4 teaspoons of sugar from tea/ coffee per day then don't add sugar; you may use sweeteners such as Splenda, Canderel, or Sweetex.
- ☒ Other suitable drinks include:

### **Skimmed milk, served chilled or hot**

Serve plain or if you are hungry try:

- Blended with fruit and yogurt
- Add cocoa and a teaspoon of sugar

### **Lower calorie instant hot drinks**

Cadbury Highlights (chocolate)

Options (variety of chocolate and other flavours)

### Alcohol

- ☒ You may drink alcohol in moderation (except on the day before your 'Heart Health' visit at St Thomas')
- ☒ Men should drink no more than 3 units of alcohol a day (maximum of 21 units in a week)
- ☒ Women should drink no more than 2 units of alcohol a day (maximum of 14 units in a week)
- ☒ A unit is:
  - half a pint of standard strength (3 to 5% alcohol by volume, ABV) beer, lager or cider
  - a pub measure of spirit
- ☒ A glass of wine is about 2 units and alcopops are about 1.5 units.



## Fats and Spreads

- ☑ Wherever possible, please only use the study spread we have provided.
- ☑ The spread can be used where you would normally use butter or margarine – on bread, crackers, melted over vegetables, in sauces and in cake or biscuit mix if baking.
- ☑ Please use the study oil provided in cooking and to make salad dressings (see recipes).
- ☑ When eating out, request foods without sauces, butter or oils added.

## Jams and Condiments

- ☑ Jams, marmalade, honey and yeast extract (such as marmite, vegemite) can be used on toast, please spread thinly.

## Sauces, Stocks and Gravies

- ☑ Sauces, stocks and gravies often contain a lot of salt, sugar or fat.
- ☑ If you have time, homemade sauces and stocks are often healthier and tastier (and you can leave out the salt).
- ☑ Commercial gravy powders and granules can be very high in salt and should be avoided or limited to a small portion eg 2-3 tablespoons per serve.

- ☑ Choose commercial sauces with reduced sugar and salt. Some examples of suitable products that can be used in smaller amounts are:

Reduced sugar and salt ketchup\*  
Reduced sugar and salt brown sauce\*  
HP Fruity sauce  
Kecap/ Ketjap Manis (sweet soy sauce)  
Thai Sweet Chili Sauce

- ☑ There are some stock cubes and powders that are low in salt, but they can be more difficult to find. Examples include:

Kallo Organic Low Salt Vegetable Stock Cubes  
Kallo Very Low Salt Chicken / Beef Stock Cubes  
Marigold Low Salt Swiss Vegetable Stock Powder

# Shopping for food – what to look for

When shopping for food in the supermarket, learn to read the label so you can choose the healthiest options.

You should look for:

- What **ingredients** make up the product
- The amount of **total fat** and **calories** in the product
- How much **saturated fat** it contains
- How much **salt** is in it
- How much **added sugar** is in the food

## What is on a label?

When you read the label on a food product, locate:

### 1. The ingredients list

Ingredients are listed in order by weight, with the biggest ingredient first.

This can help you to decide if the food is healthy option. For example, you can decide if a food is not too sugary if the ingredients list states dried fruit as an ingredient but not added sugars like honey, glucose or fructose syrup, malt.

### 2. Nutrition Information

Many foods in the supermarket will have nutrition information displayed.

The label will show the **amount per 100g or 100ml** of energy (calories), protein (grams), carbohydrate (grams) and fat (grams), as well as the amount of any nutrient where a claim has been made. Note that the figures for sugar include the sugar that comes from natural sugars (eg fruit sugar or fructose and milk sugar or lactose) as well as from added sugars (such as table sugar or sucrose).

There may also be these nutrient amounts [per serving](#), in addition to the 'per 100g' column, but the serving size may differ from brand to brand. While serving sizes can be a good starting point, remember it is your actual serving size that will affect how much sugar, fat, saturated fat and salt you will consume.

Looking at the label can help you decide whether the product contains 'high' 'medium' or 'low' amounts of fat, sugar and salt.

	Per 100g	
	A LITTLE	A LOT
<b>Fat g</b>	3g or less	20g or more
<b>Saturated fat g</b>	1g or less	5g or more
<b>Sugars g</b>	2g or less	10g or more
<b>Salt (Sodium x 2.5) g</b>	0.3g or less	1.5g or more

## EXAMPLE

In the example below, this cheese contains 21.8% fat (21.8g per 100g) and 1.8g salt per 100g. It is high in fat, saturated fat and salt.

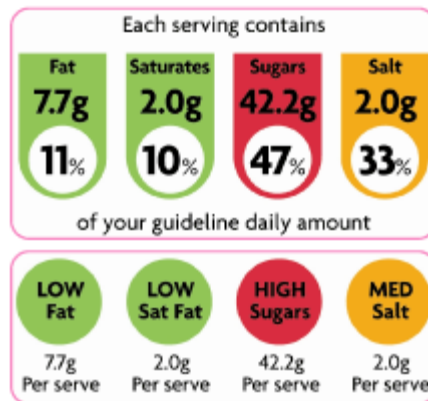
The serving size used is 30g so if you ate this much cheese you would have eaten 4.5g saturated fat and 93 calories.

### Example of nutrition information for reduced fat cheddar cheese:

NUTRITION INFORMATION	TYPICAL VALUES per 100g	TYPICAL VALUES per 30g serving
Energy	1295kJ/ 311kcal	389kJ/ 93kcal
Protein	28.6g	8.6g
Carbohydrate	0.1g	0.0g
(of which sugars)	0.1g	0.0g
Fat	21.8g	6.5g
(of which saturates)	14.9g	4.5g
Fibre	Nil	Nil
Sodium	0.7g	0.2g
Salt Equivalent	1.8g	0.5g
Calcium	960mg	288mg

### 3. 'At a glance' nutritional information on the front of packs

These are voluntary schemes aimed at providing people with a simple way for making healthier food choices.



The two main front of pack schemes in the UK are 'traffic lights' and 'GDAs'.

#### Traffic Lights

Traffic lights tell you if a food has a high (**red**), medium (**amber**), or low (**green**) amount of fat, saturated fat, sugars and salt in 100g of the food. The label will also indicate how much of these are present in one serving of the food.

Foods with a red light can be eaten occasionally, but think about how often you choose it and how much you eat at one sitting. Foods with amber lights are an okay choice, although those with green lights are even better and are the healthiest choice.

Most foods will have a mixture of red, amber and green colours but these are still useful to compare between different products to decide which is the healthier choice.

## **The ‘What’s Inside’ Guide using Guideline Daily Amounts (GDAs)**

GDAs are the amount of calories, sugars, fat, saturated fat and salt for an average adult of a healthy weight. They are not necessarily the same for everyone, and so are a guide rather than a target.

	<b>Calories</b>	<b>Sugars</b>	<b>Fat</b>	<b>Saturates</b>	<b>Salt</b>
Women	2000	90g	70g	20g	6g
Men	2500	120g	95g	30g	6g
Children 5-10	1800	85g	70g	20g	4g

The ‘What’s Inside’ guide GDA food labelling provides information for calories, sugars, fat, saturated fat and salt per serving of the food, as well as the percentage of the GDA for adult women provided by the serving. They are useful to use to compare food products to help you make healthier choices.

## Eating out and convenience meals

When you're eating out or buying food that has been prepared for you, it's easy to have too much fat, salt, added sugars and calories.

Eating out at restaurants or ordering take away food should be occasional rather than everyday. Many meals available from restaurants are higher in salt and saturated fat than home made or supermarket equivalent meals.

If you know in advance that you will be eating out, try to keep your salt and saturated fat intake as low as possible at other meals and snacks.

Fresh fruit, vegetables, unbreaded and unbattered fish or skin free chicken are naturally healthier, provided you don't add salt or sauces to them.

When ordering at restaurants, try to order:

- Menu items with sauces and dressings on the side
- A side salad, to provide one of your five a day (and is low in salt and fat)
- A side order of plain vegetables, if they are not already included in the meal.
- Avoided breaded or crumbed menu items, ask for grilled, poached, boiled or steamed.



## Restaurant meals and takeaways

When eating at restaurants or ordering takeaways, if you can't tell from the menu how a dish is cooked then ask the waiter. When you are eating out, choose the healthier options, the table below gives you some tips.

<b>Choose these:</b>	<b>Avoid these:</b>
Dishes that are: <ul style="list-style-type: none"> <li>• Grilled</li> <li>• Boiled</li> <li>• Poached</li> <li>• Steamed</li> <li>• Stir fried</li> </ul>	Dishes that are: <ul style="list-style-type: none"> <li>• Battered For example: Sweet and sour pork Scampi Battered Fish</li> <li>• Deep fried For example: Doughnuts Samosas</li> </ul>
<ul style="list-style-type: none"> <li>• Chicken without skin</li> <li>• Fish without batter</li> <li>• Prawns</li> <li>• Pulses such as lentils and beans</li> </ul>	<ul style="list-style-type: none"> <li>• Pies, pasties, sausage rolls</li> <li>• Bacon, ham, gammon</li> <li>• Sausages, frankfurts</li> <li>• Pâté</li> </ul>
Sauces based on: <ul style="list-style-type: none"> <li>• Tomatoes</li> <li>• Vegetables</li> </ul>	Sauces based on: <ul style="list-style-type: none"> <li>• Cream</li> <li>• Cheese</li> <li>• Butter</li> </ul>
Curries that are dry	Curries that are based on coconut milk
Rice that is: <ul style="list-style-type: none"> <li>• Steamed</li> <li>• Boiled</li> </ul>	Fried rice such as: <ul style="list-style-type: none"> <li>• Pilau</li> <li>• Egg fried rice</li> </ul>
Plain unfilled pasta	Pasta filled with cheese or meat
Potatoes that are: <ul style="list-style-type: none"> <li>• Baked</li> <li>• Boiled</li> </ul>	Potatoes that have added fats, cheese or cream, such as: <ul style="list-style-type: none"> <li>• Chips</li> <li>• Dauphinoise, gratins</li> </ul>
Vegetables and salads that are served plain: <ul style="list-style-type: none"> <li>• Ask for the dressing on the side or use the study-provided vinaigrette</li> </ul>	Vegetables and salads served with: <ul style="list-style-type: none"> <li>• Butter or buttery sauces</li> <li>• Oil or oily dressings</li> <li>• Mayonnaise such as potato salad and coleslaw</li> </ul>
Bread: <ul style="list-style-type: none"> <li>• Wholemeal</li> <li>• Granary</li> <li>• Brown</li> <li>• Seedy</li> <li>• Bagels</li> </ul>	Croissants and pastries
Fruit, fruit salad and sorbets	Cakes, puddings, biscuits, sweets, cream and ice cream

## **Indian (Note that Indian cuisine is very high in salt)**

Choose lower-fat options such as:

- tandoori or madras with chicken, prawns or vegetables
- plain rice and chapatti instead of pilau rice and naan
- Include a dhal



Try to avoid creamy curries such as:

- korma
- passanda
- massala

Remember for a healthy meal you should try to:

- base your meal on starchy foods, so this means choosing plain rice or chapatti
- have plenty of vegetables, so choose vegetable side dishes and a dhal

## **Italian**

If you are having pizza:

- Choose lower-fat toppings, such as vegetables, fish and prawns
- Ask for half the usual amount of cheese
- You could ask for some extra vegetables on your pizza to bump up your daily fruit and veg portions
- Share the pizza so you aren't tempted to eat the whole thing, and add a side salad



When you have pasta:

- Go for a sauce based on tomatoes or vegetables, rather than cream
- Vegetarian pasta dishes, provided they are not cream or cheese based, are often a healthier option
- Have a smaller main meal such as a starter-size pasta with a side salad or vegetables - Italian restaurants often serve two sizes of pasta dishes.
- Avoid garlic bread, which contains a lot of salt and butter. Instead have a small portion of bruschetta (a tasty bread topped with fresh tomatoes and herbs)
- 

## **Chinese (Note that Chinese cuisine is very high in salt)**

Choose lower-fat options such as:

- Steamed fish
- chicken chop suey





- Szechwan prawns
- Vegetables stir fried

Avoid anything cooked in batter.

- Sweet and sour pork is usually battered (ask if you're not sure).

Go for steamed or plain rice rather than egg-fried rice.

Avoid deep fried starters such as prawn crackers, dim sum and spring rolls.

Avoid adding soy sauce, this is very high in salt, and Chinese cuisine already contains a lot of salt.

### **Thai (Note that Thai cuisine is very high in salt)**

Try to stick to stir-fried dishes or steamed dishes containing chicken, fish or vegetables.

Avoid green and red curries, they contain coconut milk and are high in saturated fat.

**Include** steamed rice rather than fried rice or noodles with your meal.

Avoid adding soy sauce, this is very high in salt, and Thai cuisine already contains a lot of salt. Thai sweet chilli sauce is a low salt sauce that you can use instead of soy.

### **Burgers and kebabs**

If you're having a burger you can still go for the healthier option:

- Choose grilled burgers made from lean meat or fish
- Ask for your burger without cheese or mayonnaise
- Ask for extra salad

Go for a shish kebab served with pita bread and salad rather than a doner kebab. Go easy on sauces which can be high in salt.

## Convenience Meals

Ready meals and shop bought sandwiches can be high in calories, saturated fat and salt.

Preparing your own sandwiches, salads and meals at home will make healthy eating easier. You will know exactly what is in the food you eat, and you can save money at the same time.

However if you need to purchase ready prepared foods, read the label and use the guidelines below to choose the healthiest option.

### Sandwiches

Aim for a sandwich that is wholegrain (brown, wholemeal or granary bread) and has:

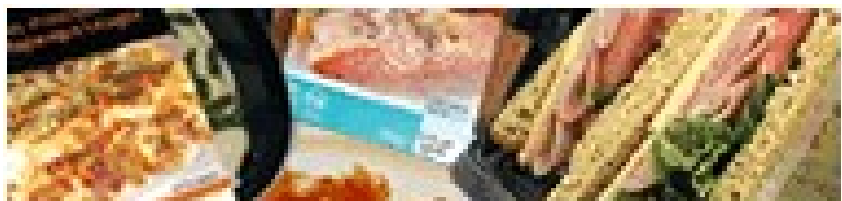
- Around 400 Calories or less
- Less than 5g of saturated fat
- Less than 1.5 - 2.0g salt per pack

Some outlets will have sandwiches with around 1.0g salt per pack, the lower the better, so choose the sandwich with the lowest salt content.

- Team with fresh fruit and a yoghurt or a plain green salad rather than crisps

If there is no nutrition information provided, here are some tips to help you choose the best sandwich:

- Go for brown, wholemeal or granary bread
- Choose chicken, turkey, salmon, prawn fillings and lean meats
- Avoid fillings with cheese, mayonnaise, bacon, pastrami and processed meats
- Try to choose a sandwich that contains salad vegetables



## Salads

Salads can be a filling and healthy choice, follow the tips below:

- Include some starchy foods such as rice, pasta, quinoa, potatoes or couscous
- Cold grilled chicken (without the skin), prawns, sardines, cottage cheese or mozzarella are all healthy choices for a salad
- Look for a variety of veg - roasted peppers and courgettes, avocado, spring onions, salad leaves, tomatoes, radishes, grated carrot, raisins or green beans.
- Avoid salads that contain a lot of mayonnaise or other dressings high in fat such as coleslaw, potato salads and some pasta salads. Only purchase these if the dressings are separate and you can leave it out.
- Pre-packed salads with nutrition information on the label allow you to choose those that are lower in fat and salt. Go for salads that are lower in saturated fat and salt

Try making your own salad at home:

- Use leftover potatoes and veg such as broccoli and green beans
- Turn leftover rice into a tasty salad

## Ready Meals

Ready Meals are not as good as cooking from fresh ingredients, but they are often a better choice than restaurant meals that may be higher in saturated fat and salt.

Aim for a ready meal that has:

- **400-600 Calories** or less
- Around **10g fat** or less
- Less than **2.0 g salt**
- **Add** some fresh **vegetables** that are steamed or boiled

**Brown rice or pasta** is a good option to bulk out the meal if you find the portions small





## Portions of fruit and vegetables



### What counts?

Fresh, frozen, chilled, canned (but not fruit in syrup), 100% fresh juice, and dried fruit and vegetables all count as a portion of fruit and vegetables.

### Fruit

- One portion of fruit is, for example, half a large grapefruit, or a slice of melon, or 2 satsumas, or 3 dried apricots or 1 tablespoon of raisins.
- A glass of 100% juice (fruit or vegetable juice) counts as 1 portion.

### Vegetables

- One portion of vegetables is, for example, 3 tablespoonfuls of cooked carrots or peas or sweetcorn, or 1 cereal bowl of mixed salad.

### Variety

To get the maximum benefits, you need to eat different types of fruit and vegetables. Fruits and vegetables all contain different combinations of fibre, vitamins, minerals and other nutrients. So aim to include a variety of fruit and vegetables to get the most benefit.

### Ready meals and takeaways

The fruit and vegetables contained in convenience foods and in takeaways - such as ready meals, pasta sauces, soups and puddings - can contribute to your daily portions of fruit and vegetables. But convenience foods can also be high in added salt, sugar or fat - which should only be eaten in moderation – so try to consume your fruit and vegetable portions from fresh produce.

Examples of portion sizes of some fruit and vegetables



12 chunks of  
canned pineapple



7 cherry tomatoes



1 medium pear



1 medium apple



1 cereal bowl of  
mixed salad



2 halves of canned  
peaches



2 satsumas



1 tablespoon of  
raisins



1 handful of  
vegetable sticks



1 handful of grapes



1 medium banana



3 heaped  
tablespoons of peas



2 medium plums



2 broccoli florets



half a large  
courgette



1 medium glass of  
orange juice



7 strawberries



3 whole dried  
apricots



Just Eat More  
(fruit & veg)



3 heaped  
tablespoons of  
sweetcorn



3 heaped  
tablespoons of  
carrots



Just Eat More  
(fruit & veg)



3 heaped  
tablespoons of  
cooked kidney beans



16 okra



## Which fish is oily and which fish is white?

These are oily fish....	These are white fish....
Anchovies *	Brill
Carp	Catfish
Eel	Cod
Herring (BLOATER)	Coley
Hilsa	Dab
Jack (also known as Scad, Horse Mackerel and Trevally)	Dover Sole
Kipper (Herring) *	Flounder
Mackerel; Smoked Mackerel*	Flying Fish
Orange Roughy	Gurnard
Pilchards	Haddock; Smoked Haddock*
Salmon; Smoked Salmon*	Hake
Sardines	Halibut
Sprats	Hoki
Swordfish	John Dory
Trout	Lemon Sole
Tuna (fresh not canned)	Ling
Whitebait	Marlin
	Monkfish
	Pangas (also known as River Cobbler, Basa or Pangasius)
	Parrot Fish
	Plaice
	Pollack
	Pomfret (also known as Butterfish)
	Red and Grey Mullet
	Redfish (also known as Ocean Perch or Rose Fish)
	Snapper (also known as Jobfish and Red Snapper)
	Rock Salmon / Dogfish (also known as Flake, Huss, Rigg or Rock Eel)
	Rohu (also known as Ruhi)
	Sea Bass
	Sea Bream (also known as Porgy)
	Shark
	Skate
	Tilapia
	Tuna (canned)
	Turbot

\* These fish are higher in salt, limit your portion size and don't eat these all the time

<b>BREAKFAST IDEAS</b>
<b>LUNCH IDEAS</b>
<b>EVENING MEAL IDEAS</b>
<b>SNACK IDEAS</b>

<b>SUMMARY OF YOUR CHANGES</b>



## **Dietary information provided to participants randomised to the conventional UK (control) dietary arm**

- 1 Your questions answered (2 pages)
- 2 Eatwell Plate overview of dietary changes (1 page)
- 3 Summary dietary information by food group (1 page)
- 4 Guidelines for alcohol (1 page)
- 5 Which fish is oily?

## **SOME OF YOUR QUESTIONS ANSWERED**

Thank you for volunteering to take part in the CRESSIDA study. Please take the time to read the enclosed leaflets, which give you advice on the changes we will be asking you to make to your diet during the study.

### **Why are we asking you make changes to your diet?**

Previous studies have looked at what happens to your risk of heart disease when you change one aspect of your diet. The aim of this study is to find out if making a number of changes to your diet in combination reduces your risk of heart disease or stroke, compared with a balanced traditional British diet.

This is not a weight loss study and you are free to eat as much or as little as you wish of other foods. We will examine whether specific changes in the types of food you eat can improve your health.

### **Why is it important that I make the changes to my diet?**

It is now widely recognised that there are links between what we eat and our health. This research project will provide important guidance on the types and quantities of foods we should be eating to improve health. We recognise that the success of the study is wholly dependent on people, like you, volunteering their time to take part. However the results we obtain will only be useful to public health recommendations if we can be sure that the dietary changes we ask you to make have been followed.

### **What support will I receive to help me follow this dietary advice?**

We will help you to follow your dietary advice by providing a number of foods we would like you to introduce into your diet. If you are unable to eat the foods we provide it is important to tell us and we will try our best to offer alternatives so that you may be able to continue to take part.



## **What changes will I have to make to my diet?**

The study will be comparing two different diets – a ‘modern’ view of a healthy diet and a more traditional view of a healthy diet. You have been allocated to a group that will follow one of these diets; this was a random process meaning that you had an equal chance of being allocated to either one of the two groups. These guidelines are specific to the group to which you have been allocated. Both of the groups are equally important to the findings of the study.

We will be asking you to eat certain foods in particular quantities, these are everyday foods and do not contain any unusual ingredients and will replace similar foods that you are likely to eat as part of your normal diet. In addition we will be asking you to avoid certain foods that you may or may not regularly eat. These changes to your diet will ensure that the types and amounts of food and nutrients in your diet match the requirements of the group to which you have been allocated. During the study we will ask you to make changes to your consumption of the following foods, some of which we will provide for you.

1. Fats - spreads and cooking oils
2. Snacks
3. Milk and milk products
4. Breakfast cereals
5. Rice/pasta /potatoes/ bread
6. Fish

You will need to continue with these changes for the whole 12 weeks of the study.

## **What if I have questions or I am having trouble following the advice?**

We want to make it as easy as possible for you to follow your dietary advice. We are available to answer your questions by phone or email. If you are unable to eat the foods we provide or have other problems which affect your ability to make the changes we have asked, it is important to tell us.

Phone numbers: 020 7848 3360 or 020 7848 4461.

Email: [cressidastudy@kcl.ac.uk](mailto:cressidastudy@kcl.ac.uk)

# The eatwell plate



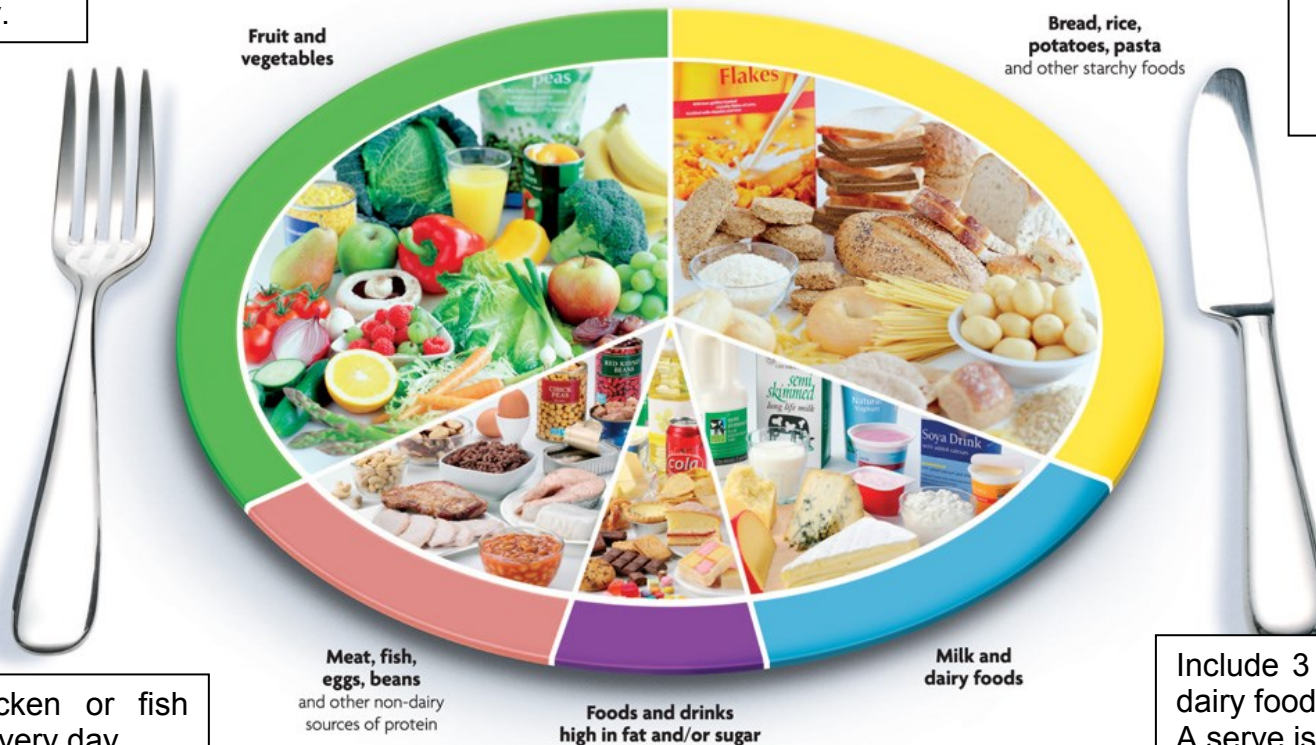
Use the eatwell plate to help you get the balance right. It shows how much of what you eat should come from each food group.

Include one piece of fruit every day.

Eat two serves of vegetables every day.

Base your meals on:

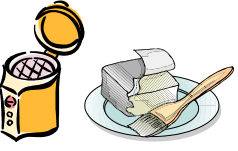

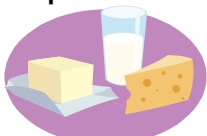

- bread
- cereals and grains
- potatoes



Include meat, chicken or fish (white fish ONLY) every day.  
- Baked beans and other pulses are a non-meat alternative.

Eat these foods in moderation.

Include 3 serves of milk and dairy foods each day.  
A serve is:  
- A glass of milk  
- A matchbox of cheese  
- A pot of yogurt

<p><b>Fats</b></p> 	<p><input type="checkbox"/> Use the <b>study</b> spread instead of your usual spread: <i>in sandwiches, on vegetables, in sauces and in baking.</i> <b><i>Aim for 2- 4 teaspoons each day</i></b></p> <p><input type="checkbox"/> Use the <b>study</b> oil instead of your usual cooking oil or as a vinaigrette <b><i>Aim for 1-2 tablespoons each day</i></b></p>
<p><b>Fish</b></p> 	<p><input type="checkbox"/> Avoid all oily fish.</p> <p><input type="checkbox"/> White fish and shellfish can be eaten freely.</p> <p>We will provide you with tins of tuna.</p>
<p><b>Milk and milk products</b></p> 	<p><input type="checkbox"/> Include three serves per day of full fat dairy products including full cream milk, yogurts, fromage frais, cheeses</p>
<p><b>Breads and starchy foods</b></p> 	<p><input type="checkbox"/> Eat only the study breakfast cereals.</p> <p>We will provide you with a choice of: Cornflakes, Special K or Rice Crispies.</p>
<p><b>Snacks</b></p>	<p><input type="checkbox"/> Eat these in moderation.</p> <p>We will provide you with biscuits and crackers.</p>

# Alcohol

- ☒ You may drink alcohol in moderation (except on the day before your 'Heart Health' visit at St Thomas')
- ☒ Men should drink no more than 3 units of alcohol a day (maximum of 21 units in a week)
- ☒ Women should drink no more than 2 units of alcohol a day (maximum of 14 units in a week)
- ☒ A unit is:
  - half a pint of standard strength (3 to 5% alcohol by volume, ABV) beer, lager or cider
  - a pub measure of spirit
- ☒ A glass of wine is about 2 units and alcopops are about 1.5 units.

## Which fish is oily and which fish is white?

These are oily fish....	These are white fish....
Anchovies	Brill
Carp	Catfish
Eel	Cod
Herring (BLOATER)	Coley
Hilsa	Dab
Jack (also known as Scad, Horse Mackerel and Trevally)	Dover Sole
Kipper (Herring)	Flounder
Mackerel	Flying Fish
Orange Roughy	Gurnard
Pilchards	Haddock
Salmon	Hake
Sardines	Halibut
Sprats	Hoki
Swordfish	John Dory
Trout	Lemon Sole
Tuna (fresh not canned)	Ling
Whitebait	Marlin
	Monkfish
	Pangas (also known as River Cobbler, Basa or Pangasius)
	Parrot Fish
	Plaice
	Pollack
	Pomfret (also known as Butterfish)
	Red and Grey Mullet
	Redfish (also known as Ocean Perch or Rose Fish)
	Snapper (also known as Jobfish and Red Snapper)
	Rock Salmon / Dogfish (also known as Flake, Huss, Rigg or Rock Eel)
	Rohu (also known as Ruhi)
	Sea Bass
	Sea Bream (also known as Porgy)
	Shark
	Skate
	Tilapia
	Tuna (canned)
	Turbot

## Appendix 3.2 Results: Biomarkers of nutrient intake

### Indices of salt, fruit and vegetable intake

Mean sodium excretion, corrected for completeness of urine collection using PABA recovery, fell by 40mmol/day in the intervention group but not the control group. Similarly mean potassium excretion was 9mmol/day higher in the cardioprotective group (Figure 1). Using the assumption that all urinary sodium relates to dietary salt intake, and a conversion of 17.1mmol of sodium being equivalent to 1g of salt (Sadler et al., 2012), then a urinary sodium excretion of 100 mmol/day would be consistent with the level expected if dietary salt intake was less than 6 g/day. Mean sodium excretion was 93 mmol/day on the cardioprotective diet and 142 mmol/d on the control diet (equivalent to dietary intakes of 5.4 g and 8.3 g salt respectively).

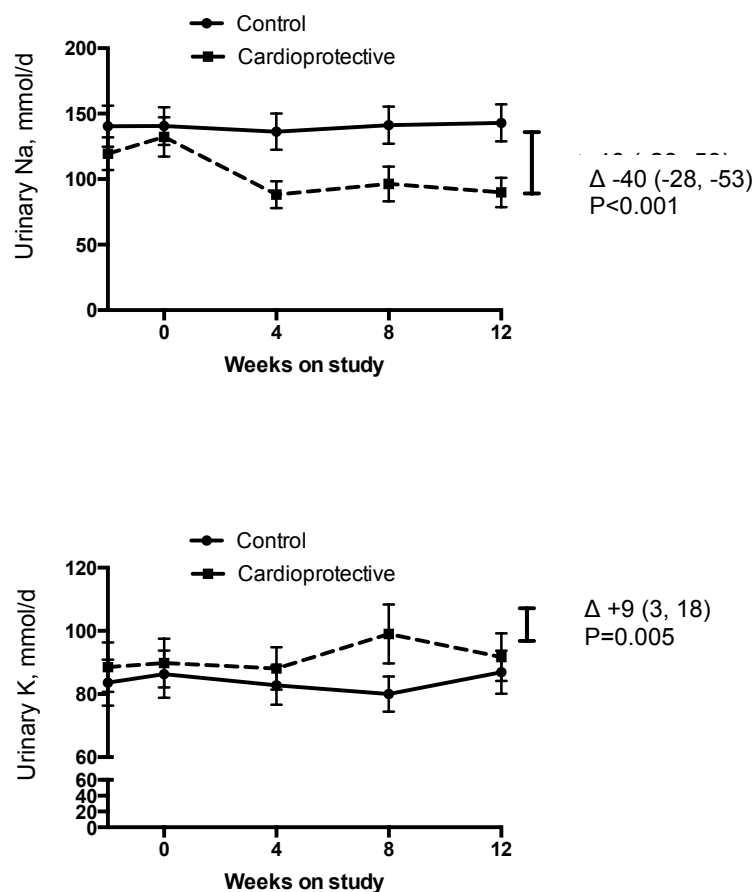


Figure 1 Change in 24-hour urinary sodium (upper panel) and potassium (lower panel) excretion on treatment adjusted for completeness of collection using PABA recovery  
Values are mean with 95% CI. Na, sodium; K, potassium; CI, confidence interval;  $\Delta$ , mean change adjusted for baseline value.



## Indices of whole grain intake

Total concentrations of plasma alkylresorcinols were about 40% higher following the intervention compared with the control diet and the concentration of serum folate fell by 16% on the intervention (Table 1). The higher alkylresorcinol results indicate compliance with cardioprotective dietary advice to increase the intake of wholegrain cereals, and the higher serum folate in the control group was due to the fortification of non-wholegrain breakfast cereals with folic acid.

Table 1 Plasma alkylresorcinol (AR) and serum folate concentrations

	Cardioprotective <sup>1</sup>	Control <sup>2</sup>	% Difference	<i>P</i> value <sup>3</sup>
<b>Total AR (nmol/L)</b>				
Baseline	80.3 (68.1, 94.6)	80.3 (68.1, 94.6)		
Endpoint	92.9 (78.7, 109.7)	70.2 (59.3, 83.1)	40 (22,59)	0.001
<b>AR C17:0 (nmol/L)</b>				
Baseline	0.9 (0.7, 1.2)	0.9 (0.7, 1.1)		
Endpoint	0.9 (0.8, 1.2)	0.7 (0.6, 0.8)	35 (13,56)	0.002
<b>AR C19:0 (nmol/L)</b>				
Baseline	13.5 (11.3, 16.3)	12.1 (10.0, 14.6)		
Endpoint	14.5 (12.1, 17.5)	10.3 (8.5, 12.4)	39 (19,59)	0.001
<b>AR C21:0 (nmol/L)</b>				
Baseline	39.5 (33.4, 46.7)	40.8 (34.5, 48.3)		
Endpoint	45.9 (38.7, 54.6)	35.9 (30.1, 42.7)	37 (18,56)	0.001
<b>AR C23:0 (nmol/L)</b>				
Baseline	17.7 (14.8, 21.2)	20.2 (16.9, 24.3)		
Endpoint	21.3 (17.9, 25.3)	16.4 (13.8, 19.5)	39 (19,59)	0.001
<b>AR C25:0 (nmol/L)</b>				
Baseline	6.2 (5.1, 7.4)	6.6 (5.4, 7.9)		
Endpoint	7.3 (6.1, 8.7)	5.2 (4.3, 6.2)	39 (19,60)	0.001
<b>Serum folate (µg/L)</b>				
Baseline	8.3 (7.6, 9.1)	7.6 (6.9, 8.3))		
Endpoint	7.9 (7.3, 8.6)	8.7 (8.0, 9.4))	-16 (-25,-7)	0.001

Values are geometric means or treatment effects (%) with 95% CI

<sup>1</sup> n=80, <sup>2</sup> n=82, <sup>3</sup> Data were log<sub>e</sub> transformed prior to analysis; probability is from analysis of covariance with the baseline value as covariate

## Indices of oily fish intake

The proportion of eicosapentaenoic (EPA) and docosahexaenoic (DHA) acids in erythrocyte lipids increased in the cardioprotective group, indicating compliance to advice to increase portions of

oily fish per week (Figure 2). Additional analyses were conducted on plasma lipids and showed similar changes (data not shown).

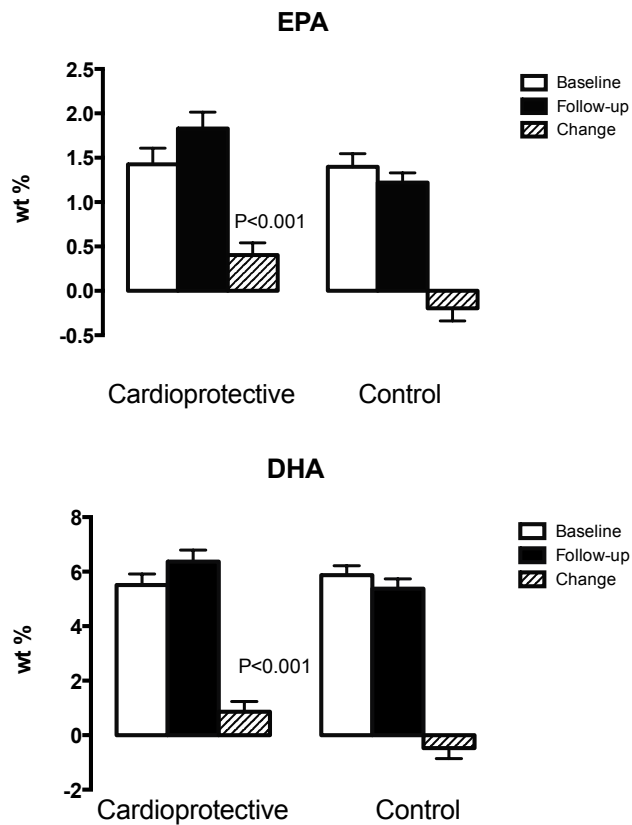


Figure 2 Change in eicosapentaenoic acid (EPA; 20:5n-3) and docosahexaenoic acid (DHS; 22:6n-3) in erythrocyte lipids before and after intervention

## Indices of added sugars intake

The cardioprotective group showed significantly lower (64%) urinary sucrose excretion compared with the control group, indicating compliance with dietary advice to restrict the intake of added sugars (sucrose). There was a tendency for fructose excretion to be lower but this did not achieve statistical significance ( $p=0.08$ ) when adjusted for PABA recovery (Table 2).

Table 2 Urinary sucrose and fructose adjusted for completeness of collection as assessed by PABA recovery

	Cardioprotective		Control		% Difference <sup>2</sup>	P value
<b>24h urinary sucrose corrected for PABA recovery (μmol/24h)<sup>1</sup></b>						
Baseline	n=71	41.3 (30.4, 56.0)	n=78	44.1 (34.4, 56.4)		
Midpoint	n=74	25.1 (18.5, 34.2)	n=73	54.3 (40.4, 73.1)		
Endpoint	n=60	20.9 (13.7, 31.7)	n=64	59.0 (47.5, 73.3)		
Mean on treatment	n=75	28.5 (21.5, 37.7)	n=80	61.6 (49.1, 77.3)	-64.2 (-96.6, -31.9)	<0.001
<b>24h urinary fructose corrected for PABA recovery (μmol/24h)<sup>1</sup></b>						
Baseline	n=71	44.3 (31.8, 61.5)	n=78	36.8 (25.5, 53.2)		
Midpoint	n=74	32.7 (22.4, 47.5)	n=73	42.4 (29.6, 60.6)		
Endpoint	n=60	21.3 (13.4, 33.8)	n=64	44.1 (31.8, 61.2)		
Mean on treatment	n=75	34.3 (24.1, 48.7)	n=80	49.7 (36.7, 67.4)	-36.5 (-77.8, -4.7)	0.082

<sup>1</sup>Geometric means with 95% CI. <sup>2</sup>Mean difference with 95% CI adjusted for baseline values, age, BMI, gender and ethnicity.

## Appendix 3.1 References

Sadler, K., Nicholson, S., Steer, T., Gill, V., Bates, B., Tipping, S., Cox, L., Lennox, A. & Prentice, A. (2012) National diet and nutrition survey - Assessment of dietary sodium in adults (aged 19 to 64 years) in England, 2011. London, Food Standards Agency.